THE DIFFUSING CAPACITY OF THE LUNGS IN COALMINERS' PNEUMOCONIOSIS.

A thesis submitted for the Degree of Doctor of Medicine in the University of Edinburgh

by

RONALD STEWART McNEILL
M.B., Ch.B., M.R.C.P.E.

September, 1959.

<u>Table of Contents</u>

	Page
Introduction	1
Methods.	
Subjects, history, examination, investigation	11
Tests of pulmonary function	21
Lung volumes	22
Ventilatory efficiency	25
Lung compliance	30
Diffusing capacity	32
Results.	
General	41
Diffusing capacity	46
Ventilatory function	66
Lung volumes	76
Lung compliance	89
Blood findings	91
Summary of results	99
Interrelation of tests	102
Discussion.	
Selection and characteristics of subjects	112
Diffusing capacity: principles, measurement, errors	125
results	143
Ventilatory function	157
Lung volumes	161
Lung compliance	163
Blood findings	165
Summary	168
Acknowledgements	170
References	171
Appendix: Mining environment in Fife coalfields	
Tables	

INTRODUCTION

During the past twenty years a great deal of work has been directed towards determining the cause of disability in coalminers' pneumoconiosis. Notable contributions have been made in America and Europe but none has been so comprehensive and meticulous in method as the report by Gilson and Hugh-Jones (1955) to the Medical Research Council on "Lung Function in Coalworkers' Pneumoconiosis". Based on the work done by their colleagues and themselves in the previous 6 years in the Pneumoconiosis Research Unit in South Wales, they came to the conclusion that breathlessness, which is the principal symptom of the disease, can best be explained by a reduction in ventilatory capacity of the lungs, that is, their capacity to shift air in and out at speed, associated with an increased ventilatory requirement on exercise. This conclusion was not based, as many conclusions by others have been, on a single test of lung function but on estimations of lung volumes, ventilatory efficiency including evenness of distribution of inspired gases, gas transfer within the lungs, and arterial blood studies at rest and after exercise. The results were related to the variables of age, radiological stage of the disease and disability in so critical and comprehensive a fashion that for a time it appeared that this study had answered all the important questions about the disorder of lung function brought about by pneumoconiosis. Gilson and Hugh-Jones found that the ventilatory capacity was better related to an independent assessment of breathlessness than any other of their tests and this has led Carpenter, Cochrane, Gilson and Higgins (1956) to substitute the ventilatory capacity for an estimate of the degree of dyspnoea, and many others to use some measure of this capacity as the sole test of lung function.

But dyspnoea in miners with pneumoconiosis cannot always be explained by an impairment of the ventilatory capacity and Gilson and Hugh-Jones also reported an increase in the amount of air required for a given amount of exercise, especially in the more advanced stages of the disease, which they associated more with unevenness of pulmonary ventilation and an overall impairment of gas transfer. Furthermore, with the development of more specific tests of lung function which Gilson and Hugh-Jones were unable to include, it has become desirable to reinvestigate pneumoconiosis so that all the possible causes of disability may be disclosed. Recently

Lethart (1959) reported the results of a detailed study of the mechanical properties of the lungs. He found that although the lungs were stiffer than normal in the later stages of the disease when progressive massive fibrosis had developed, in simple uncomplicated pneumoconiosis they were only slightly stiffer than normal and the degree was unlikely to be clinically significant. It may be, however, that disability arises from the sum of different functional disorders each in itself insufficient to be causative and in this respect the impairment of gas transfer, referred to by Gilson and Hugh-Jones, deserves further consideration. They reported a slight impairment in simple pneumoconiosis and a moderate impairment in advanced complicated pneumoconiosis and indeed, when one considers the nature of the disease this is hardly surprising. Heppleston (1954) has examined the lungs of miners killed at work and he described an even distribution of coal dust on the alveolar walls and other air passages in the process of being engulfed by phagocytes. Normally the dust is then carried to the lymph spaces around the respiratory bronchioles or through the alveolar walls to the interstitial spaces but, despite the efficient and rapid mechanisms for handling dust, silting up can be seen within the alveoli themselves. He described the development of the focal lesion of simple pneumoconiosis to the stage where the respiratory bronchiole is closely invested by a broad cylinder of dust cells consolidating the pre-existing vesicular tissue (Heppleston 1947, 1954). In such a situation even before the development of confluence and progressive massive fibrosis, there are good grounds for supposing that there is an interference with the normal diffusion pathway of gases between alveolus and capillary blood in the affected areas and an overall reduction of the surface area available for diffusion within the lungs.

Two gases are suitable for the measurement of diffusion, oxygen and carbon monoxide. The measurement is easier with carbon monoxide but as yet the only important study reporting its use in pneumoconiosis of coalminers is that by Gilson and Hugh-Jones (1955). They measured the percentage uptake of carbon monoxide by the lungs, by comparing the concentration of the inspired and expired gas, after the subject had reached a steady state when breathing the special gas mixture. Theoretically this method has the obvious objection that it gives values which depend both on the amount of ventilation and on the ability of the lungs to take up carbon monoxide. Thus the percentage of carbon monoxide removed from the inspired gas will approach zero either as the tidal volume decreases towards a volume sufficient to ventilate the dead space only, or as the ventilation increases to such an extent that the mean alveolar concentration of the gas is maintained at, or very close to, the concentration of the inspired mixture. The maximum percentage uptake will lie between these limits. Gilson and Hugh-Jones realised these objections and partially corrected for them (as will be discussed later) but it is undesirable to base final conclusions about the efficiency of gas transfer in pneumoconiosis on this method when more precise ones are now available.

Motley, Lang and Gordon (1950) using oxygen, have made the other important study on gas exchange in anthracite coalminers in Pennsylvania, U.S.A. While apparently obtaining the data necessary for the calculation of the diffusing capacity of the lungs for oxygen they neither quote the data nor make the calculations, but state generally that the alveolar to arterial oxygen tension gradient decreases while breathing a low concentration of oxygen and increases while breathing a higher than normal concentration, thus indicating that no true diffusion defect resides in the alveolar membrane.

While this conclusion may be valid it is unsatisfactory as no values are supplied which can be compared and related to the variables of age and radiological stage of the disease.

It was therefore decided to investigate the diffusing capacity of the lungs in coalminers' pneumoconiosis and to express it in terms of millilitres of gas that can be transferred per minute per millimeter of mercury pressure gradient between the alveolus and capillary blood. For convenience the gas chosen was carbon monoxide and the method, which is discussed later, is the single breath one of Ogilvie, Forster, Blakemore and Morton (1957). To avoid the pitfall of estimating only one function of the lung and forgetting parallel disturbances, the subject was studied as fully as possible. The interrelation of the diffusing capacity with other tests of lung function and with disability, age and radiological category forms the basis of this thesis.

Undoubtedly the major difficulty that arose was the selection of the cases for study. The studies were done in Maryfield Hospital, Dundee, but there are no coal-fields in the County of Angus. Bridge of Earn Hospital in the neighbouring County of Perth has a small Industrial Chest Diseases Unit which serves the Fife coalfields. The stimulus for the study came therefore by the indirect route of a commitment to the Unit at Bridge of Earn. The persistent and salutary warnings from the Pneumoconiosis Research Unit in South Wales about the importance of random sampling from a defined population in the study of a disease such as pneumoconiosis, almost paralysed action from the start. In default of the impeccable facilities that exist in South Wales, an effort has been made to compensate for the obvious difficulty in selection, and in fact at least half of the subjects studied avoid the serious objections of hospital selection. When the results of these and the others are compared later, it will be seen that there is remarkably little difference between them. Furthermore, it is surely also important to discover qualitative changes that may occur in a disease without concluding that such changes are invariable. The danger is that abnormal findings may be attributed to the disease, which really arise from an associated disease such as bronchitis, or some other factor such as ageing. Here an attempt has been made to give due consideration to the effects of all the recognisable variables.

The study has possibly another contribution to make in that it is from Scotland. Gilson and Hugh-Jones (1955) say that from radiological surveys in Great Britain there is little doubt that when coalworkers' pneumoconiosis occurs the pathological process is the same anywhere as that seen in South Wales. Heppleston (1951) confirms this in a report on post mortem studies of 8 Scottish miners from the Lowlands. Nevertheless more evidence is desirable and in a recent report on post mortem findings in miners from the Cumberland coalfields, Faulds, King and Nagelschmidt (1959) question the very existence of progressive massive fibrosis in that area and state that silicotic nodulation is more frequent there than in South Wales. Such differences may well give rise to different functional disturbances in the lungs and they illustrate the dangers of overlooking geographical and geological factors.

In the last century, Scotland's contribution to the medical literature on pneumoconiosis was impressive. Meiklejohn (1951) has given the history of the disease in Great Britain and it is evident that many of the early clinical descriptions and important deductions about the nature of the disease were made in Scotland. Thus Gregory (1831) in Edinburgh, was the first to record that the disease arose out of employment in the coal mines. He also (with Christison) demonstrated in a brilliant and empirical manner by incinerating the black lungs of a miner obtained post mortem, that gases could be produced which burned and were similar in all respects to the distillation products of coal. Marshall (1834) in Cambuslang, near Glasgow, accepted these ideas and unequivocally concluded that the disease was a consequence of inhalation of coal particles fine enough to be inhaled without causing immediate irritation. Craig (1834) in Glasgow, was far ahead of his time in examining the distribution of black material in the lungs by slicing thoroughly dried specimens in a manner strikingly similar to that of Gough and Wentworth (1949) in present times. Others in Scotland contributed and from their impetus, action undoubtedly resulted which improved the mining environment and shortened the working hours of the miner. By 1888 Nasmyth, writing about conditions in Fife, was to state, albeit prematurely, "that conditions connected with miners' occupation are as favourable to health as those in the occupation of any other workman".

It may have been this false sense of security that produced the long silences from Scotland in the next fifty years. Hall (1937) has written about the clinical findings in Lanarkshire miners and Black (1953) has given a valuable analysis of the records of the Pneumoconiosis Medical Panel of the Ministry of National Insurance dealing with claims for disability over the years 1944-1949. Apart from this, little has been written and certainly no physiological studies have been reported. These have of course been done and part of the pneumoconiosis field research programme of the National Coal Board is in Scotland. Valuable information concerning prevalence and attack rate of pneumoconiosis in selected pits,is accumulating and physiological and environmental studies follow closely. We await the results of these long term studies,and meanwhile it is hoped that this report provides some useful information about the nature and degree of pulmonary disability in a group of miners with pneumoconiosis from the Fife coalfields.

METHODS

Subjects

All the miners in this study were from the Central Fife and East Fife coalfields, except three. One of these was from the neighbouring coalfield of Clackmannan and the other two were from Falkirk which is in the North Lanarkshire coalfield.

Fifty two were finally accepted as suffering from coalminers' pneumoconiosis on the basis of the radiological appearances of the lungs and the industrial history. The miners travelled to Dundee for the day of study only and during this day an effort was made to achieve as complete an assessment as possible of their clinical state and pulmonary function.

In the selection of the miners the net was cast as wide as possible in order to avoid the exclusive study of those who were in hospital on account of pneumoconiosis. They came from four different sources and the first two, which included half the total number studied, largely avoided the serious objections of hospital selection.

1. Sixteen miners came from the Fitness Centre, Bridge of Earn Hospital. They were there because of some orthopaedic disability or the effects of a traumatic

injury except one who suffered from mild angina pectoris. An attempt was being made to rehabilitate them for employment. None was there on account of respiratory disease.

Pneumoconiosis was diagnosed by a routine chest X-ray of all miners passing through the Centre, and the individual cases were studied as they arose, without any selection.

2. Ten working miners were selected at random from a list of known pneumoconiotics of X-ray category 2 or more, by the Fife Area Medical Officer of the National Coal Board.

   The miners attended from their homes and made the journey to Dundee for the investigation only. This arrangement was made through the good offices of the Scottish Divisional Medical Officer, Dr. C. G. Gooding, and it involved the payment of a day's wage and travelling expenses to the miner by the National Coal Board.

3. Twenty-two miners came from the Industrial Chest Diseases Unit, Bridge of Earn Hospital, where they had been referred for assessment or treatment by other doctors. Most of the miners were there for short term assessment only. The Unit had recently opened and the policy was to encourage the reference of

miners for short term investigation only, in order to make it as widely known as possible to the mining community in Fife.

Those who attended for special studies at Dundee were not selected in any way but came whenever the necessary time was available.

4. Four miners came from Glenlomond Hospital, Kinross, where they had also been referred for assessment or treatment. This Hospital has been extending its interest to all respiratory diseases whereas formerly it was concerned with tuberculosis only.

Table I in the appendix gives details of all the miners studied including their source and associated diagnoses.

Rejects. Four miners who were studied are not included in this report. Two were finally considered by independent observers, to have insufficient radiological evidence for the diagnosis of pneumoconiosis. The third was considered to be suffering primarily from pulmonary tuberculosis with little or no radiological evidence of dust, and the fourth had simple pneumoconiosis complicated by a carcinoma of the right upper lobe bronchus.

Industrial History

A full occupational history was taken but in view of the habit in Scotland of changing jobs underground, it was difficult to get precise information about employment over the years. This was, however, recorded to the best recollection of the miner, particularly in respect of time spent solely or predominantly on stone work within the mines. Most of the men had entered the mines at 14 years of age and the rest only a year or two later.

Usually they had spent a lifetime underground, but a few had had periods of unemployment or periods in the armed services. Others had been given surface or other approved employment in the mines after the diagnosis of pneumoconiosis had been made, and a very few were so disabled that they were no longer working.

In no case could any employment other than coalmining be considered as a possible cause for pneumoconiosis. In the appendix there is a description of the environmental conditions in the Fife coalfields and an indication of the prevalence of the disease.

Table II in the appendix also gives information about age, X-ray category and industrial history of each miner.

Clinical History

A full medical history was taken, but particular attention was paid to the symptoms of respiratory disease and smoking habits.

Dyspnoea. This was graded according to the method used by the Pneumoconiosis Research Unit, Cardiff (M.R.C. report No. 290, 1955). The only modification was to combine grades 0 and 1.

1. Subject's breathing as good as other men of his own age and build, at work, on walking and on climbing hills and stairs.
2. Subject able to walk with normal man of his own age and build on the level, but unable to keep up on hills and stairs.
3. Subject unable to keep up with normal man on the level, but able to walk about 1 mile or more at his own speed.
4. Subject unable to walk more than about 50-70 yards on the level without a stop.
5. Subject obviously breathless on talking or undressing or unable to leave his home because of breathlessness.

In 5 subjects only a provisional dyspnoea grading was given because they suffered from another disability that prevented a genuine assessment. Three of these had suffered from injuries 3-6 months previously and were given the dyspnoea grade that obtained prior to injury. One suffered from chronic rheumatoid arthritis and was arbitrarily graded category 3. The fifth suffered from angina pectoris and was graded according to his performance before the onset of angina nine months previously. The provisional gradings are indicated on Table I in the appendix along with the associated diagnoses.

Chronic Bronchitis. The criteria used for this diagnosis were based on those of Higgins, Oldham, Cochrane and Gilson (1956) but were slightly more strict. The diagnosis required a history of a productive cough occurring on rising in the morning and during the rest of the day, for at least three months in the year, and the history of chest illness sufficient to keep the subject off work for more than one week, occurring at any time in the past three years. If the subject attributed such a chest illness to pneumoconiosis rather than to bronchitis this was still accepted, as it was thought that this would be a likely interpretation by any pensioner.

Smoking Habits. In order to obtain more precise information about these habits a quantitative grading was followed. To equate cigarette with pipe smoking the quantities are expressed in grammes of tobacco per week, one cigarette being equivalent to 1 gramme of tobacco. The gradings were:-

S1 - 1-69 G. tobacco per week

S2 - 70-139 G. tobacco per week

S3 - 140 G. or more of tobacco per week

O.S. - non-smoker

E.S. - an ex-smoker of grade S2 or more for as long as 10 years at any period in the past

In two subjects the information obtained was imprecise and they were arbitrarily allotted to grade E.S. which is the least definite of the grades.

Physical Examination

This included all systems but again emphasised the respiratory and cardiovascular, the main object being to detect associated disease that might significantly influence the results of the pulmonary function tests.

Body Measurements. These are required for the calculation of predicted normal values for the pulmonary function tests. Height was measured to the nearest half inch with the subject in stockinged soles and weight to the nearest half pound with the subject in stockings, trousers and shirt. Surface area was calculated in square meters from the standard nomogram of Dubois and Meek (Consolazio et al., 1951).

Additional Investigations

Electrocardiogram. This was done on 44 of the 52 miners. Lack of time was the only reason for omitting the other 8. The standard limb leads, unipolar limb leads and seven precordial leads (V_3R and V_1 to V_6) were included. The tracings were interpreted by a cardiologist, Dr. H. Watson, Department of Medicine, University of St. Andrews, who had no other information about the subjects.

Haematology. This included the standard measurements of haemoglobin, packed red cell volume, red and white blood cell counts. Haemoglobin was measured by the oxy-haemoglobin method using a photoelectric E.E.L. colorimeter standardised by haemoglobin samples supplied by the M.R.C. The error associated with this instrument is 2%. These measurements were done by the Haematology Laboratory of Maryfield Hospital.

CO_2 content of venous plasma. This was measured on a manometric Van Slyke apparatus on which duplicate estimations can be achieved to within 0.2 mM/litre. The venous blood was drawn, usually without the use of a tourniquet, into a heparinised syringe with the usual anaerobic precautions, and the red cells separated as soon as possible. If a tourniquet had to be used it was kept on for as short a time as possible.

Radiology. Full sized postero-anterior and right lateral films were taken on all subjects on the day of investigation. The films were interpreted and graded separately by two skilled observers, Dr. J. McLeod, radiologist, Bridge of Earn Hospital and Dr. Stewart Rae, Medical Officer in charge of No. 1 Research X-ray Unit of the National Coal Board. It was known to both of them that the film was of a miner already diagnosed as suffering from pneumoconiosis, but despite this, three were rejected as not having the basic dust pattern. No details of disability or pulmonary function were provided. When different categories were suggested by the observers, the films were reviewed by both together and final agreement reached.

The categories of pneumoconiosis adopted are those currently accepted by international agreement (International Labour Office 1953). This recognises a distinction between simple and complicated pneumoconiosis. Simple pneumoconiosis which is a pattern of minute opacities, is divided on a quantitative basis into three categories increasing in degree of profusion from one to three. Category 0 indicates that the film is within normal limits. Complicated pneumoconiosis or progressive massive fibrosis (P.M.F.) is classified into four categories, A, B, C and D, and always occurs on a background of simple pneumoconiosis. These four categories are:-

A. Localised ambiguous shadows similar to those seen in tuberculosis.

B. One or more massive shadows of uneven density and outline.

C. Large massive shadows clearly defined and of even density.

D. Massive shadows as in C, but with gross distortion of the general anatomy of the lung, including mediastinal displacement, kinking of the trachea, tenting or haziness of the diaphragm outline and large translucent areas in the lung parenchyma.

The coding system follows that used by the Pneumoconiosis Research Unit, Cardiff, and the two arabic numbers which follow the letter indicating a complicated category are separated by a stroke and indicate the number of anterior rib spaces in the right and left lung fields respectively over which the massive fibrosis extends.

Tests of Pulmonary Function

1. Lung volumes
2. Ventilatory efficiency
3. Lung compliance
4. Diffusing capacity

All the tests of pulmonary function that have been done are described under these four headings. They are not in the order in which the results are presented later. The reason for this is that it is easier to describe the more complicated tests of function if the basic terminology and measurements are described first. Thus, although the diffusing capacity of the lungs is the main consideration of the thesis, its measurement is described last.

In all the tests the subject was at rest in the sitting position. The gas volumes were recorded at room temperature saturated with water vapour and were corrected to body temperature and pressure saturated (B.T.P.S.) unless otherwise stated.

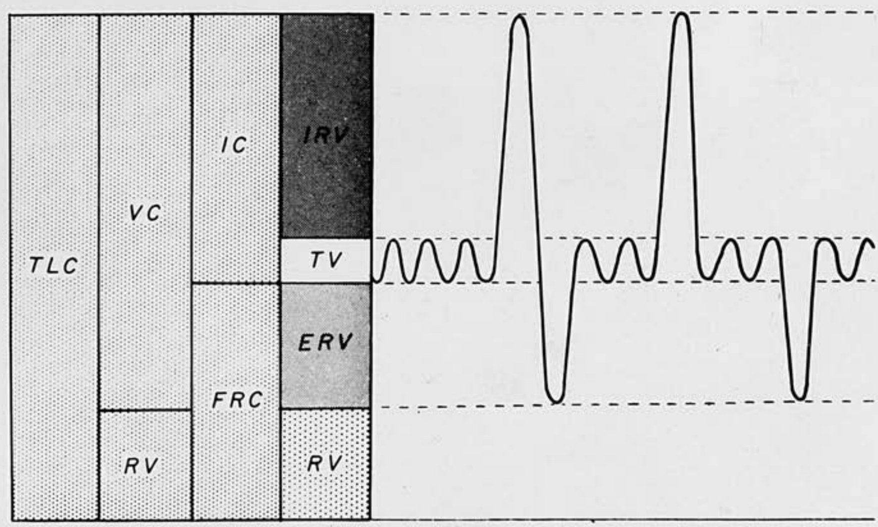
1. Lung Volumes

The subdivisions of lung volume have been named according to standard terminology (Pappenheimer et al., 1950; Comroe et al., 1955).

The vital capacity (V.C.), inspiratory capacity (I.C.) and expiratory reserve volume (E.R.V.) were all measured separately and the best of three trials was the accepted value. For these measurements the apparatus used was a spirometer made to the specifications of Bernstein, D'Silva and Mendel (1952). There were no valves and no carbon dioxide absorber in the system.

The residual volume (R.V.) was measured by the closed circuit and gas dilution method of Herrald and McMichael (1939). Helium (He), which is an inert and insoluble gas, was used in the measurement and the apparatus consisted of a Benedict-Knipping spirometer with an electrically driven pump circulating the gases in a closed circuit from the spirometer, through a CO_2 absorber and back to the mouth piece. The main stream of gas circulated at a rate of 30 litres per minute but there was a small side circuit passing gas through a helium katharometer at a flow rate of 2 litres per minute. The helium katharometer was supplied and calibrated by the Cambridge Instrument Company for He in moist air over the 0-15% range.

Figure 1



The subdivisions of lung volume after Comroe et al. (1955).

The concentrations are indicated on an eight inch scale which can be read to 0.02% He and the overall accuracy of the instrument is ± 0.1% He.

The procedure was as follows:- A known volume of 100% He was added to the spirometer which was half filled with air, and from the resulting dilution (usually to about 10% He) the total volume in the spirometer and circulating system was calculated. The subject was then switched into the circuit at the end of a quiet expiration and he rebreathed until an equilibrium of the He between the circuit and his lungs was reached. This was taken to be when the He concentration failed to fall any further after two consecutive half minutes or after a rebreathing time of five minutes, whichever was the longer. From the final dilution of He it is possible to calculate the volume in the subject's lungs when he was added to the circuit (i.e. the functional residual capacity or F.R.C.). An E.R.V. was recorded on the spirometer immediately after the final He reading was taken and if this volume is subtracted from the F.R.C. the R.V. is obtained (F.R.C.-E.R.V. = R.V.). During the period of rebreathing, the CO_2 produced by the subject was absorbed and the O_2 he consumed was replaced by oxygen from a cylinder at a rate which kept the total volume constant. A correction was made if the subject was switched into the circuit either just before or just after the end of a quiet expiration as this adds to the true F.R.C. value. The dead space volume from the "switch in" valve to the mouth (50 ml.) was subtracted for the same reason.

In 45 of the 52 subjects duplicate measurements of the R.V. checked to within 10% and the average value was accepted. In the remaining seven, time did not permit repetition of the test and the better technical performance was accepted.

The normal values for the subdivisions of the lung volumes have been taken from Needham, Rogan and McDonald (1954). As these workers did not correct their values to B.T.P.S., an adjustment was made in figures in accordance with their statement that the ambient temperature of their laboratory was around a mean of 20°C. Furthermore their equation for predicting the total lung capacity (T.L.C.) gives values which are unreasonably high and therefore, this has been derived simply by adding the predicted values of the R.V. and V.C.

2. Ventilatory Efficiency

The assessment of this lung function depended on the analysis of forced expiratory and inspiratory spirograms (F.E.S. and F.I.S.). The apparatus used was the low resistance spirometer of Bernstein, D'Silva and Mendel and a fast kymograph moving at a rate of about 4 cm. per sec.

The procedure was to record three separate F.E.S. and three separate F.I.S. The best performance was accepted for measurements which were:-

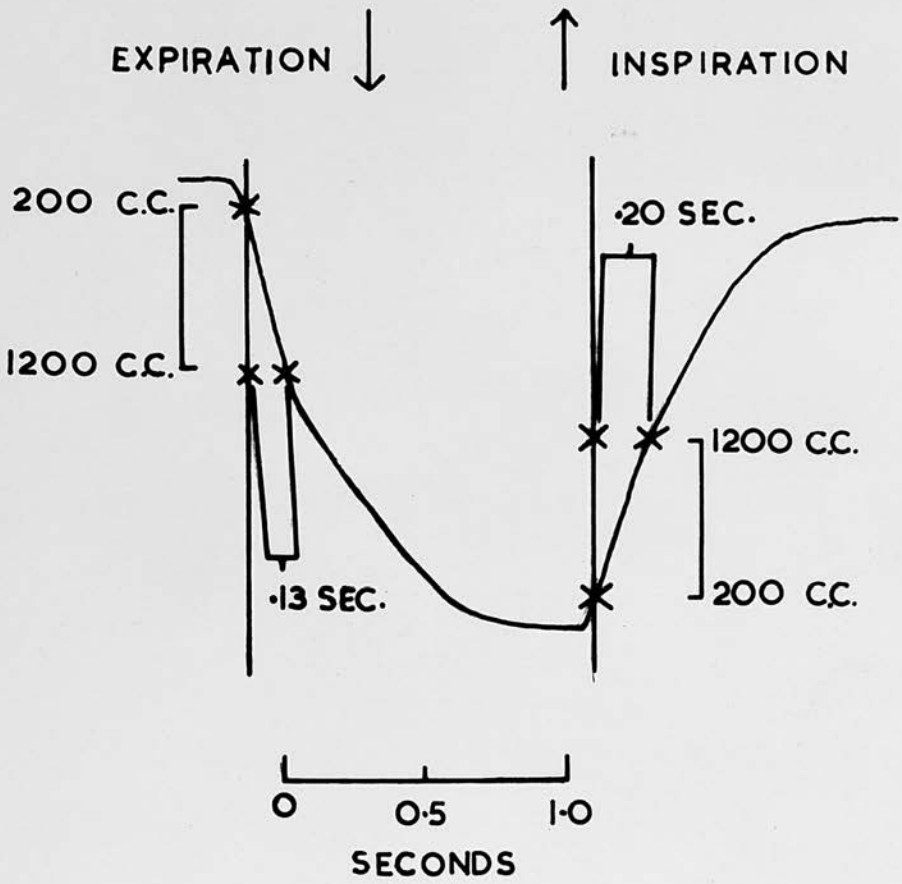
(a) The volume expelled in the first 0.75 sec. of the F.E.S. was converted to B.T.P.S. and multiplied by a factor of 40. The result is expressed in litres per minute and the value closely approaches the maximum voluntary ventilation measured over 15 seconds (Kennedy, 1953). According to the terminology recommended by Gandevia and Hugh-Jones (1955) this is referred to as the indirect maximum breathing capacity (Ind. M.B.C.).

(b) The times taken to expel and to inspire the litre of gas between the 200 and 1200 ml. points on the F.E.S. and F.I.S. were measured and these rates converted to litres per minute at B.T.P.S. This method of calculating the maximum expiratory and inspiratory flow rate (M.E.F.R. and M.I.F.R.) spirographically was first introduced by Comroe and Danzig and it is described by Comroe, Forster, DuBois, Briscoe and Carlsen in The Lung (1955). By using a rapid kymograph they claim an accuracy comparable to an electrical pneumotachograph at rates of air flow up to 400 litres per minute. The reason for rejecting the first 200 ml. on the spirogram is to avoid starting errors due to the inertia of the system.

McNeill, Malcolm and Brown (1959) found that it was only a little more difficult to instruct subjects in the performance of an F.I.S. as compared with an F.E.S. and that the coefficients of variation within trials on the same subject were of the same order (12-16%). The ratio between M.E.F.R. and M.I.F.R. was also calculated for each subject as the same authors consider that this is of value in detecting the underlying nature of a ventilatory defect. Figures 2 and 3 show the method of measuring the M.E.F.R. and M.I.F.R. and the type of tracing obtained from a subject with no ventilatory difficulty and from one with severe difficulty.

Normal values. For the Ind. M.B.C. the predicted normal values are based on those obtained by McNeill and McKenzie (1958). The regression equation is Ind. M.B.C. (L/min.) = -1.75 age in yrs + 195. There is a very close correlation (r = 0.97) between these values and the ones given by Needham et al. (1954) for the M.B.C. measured directly. However, as the former were obtained by exactly the same method and apparatus which was used in

Figure 2



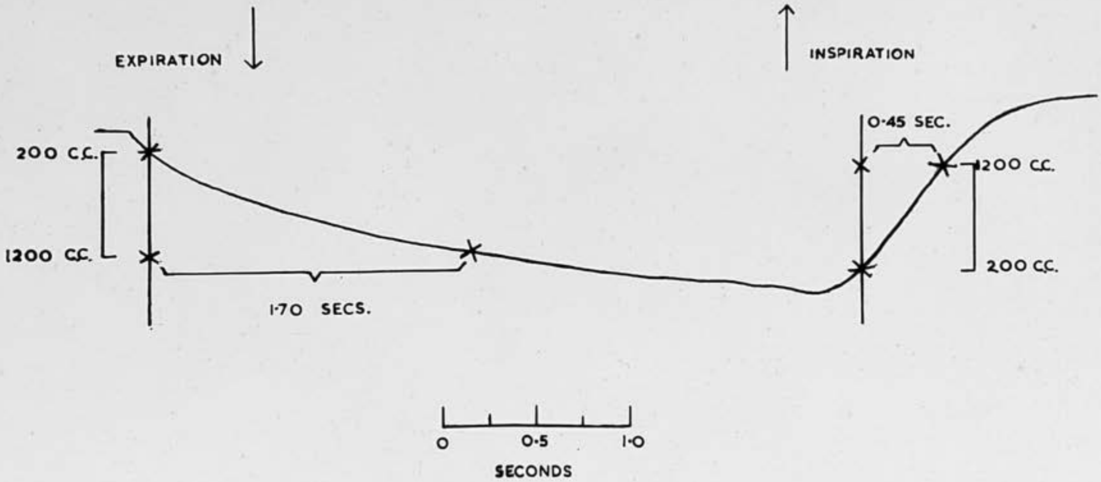
Normal forced expiratory and inspiratory spirograms shown together for convenience.

$$\text{M.E.F.R.} = \frac{1}{0.13} \times 60 = 462 \text{ L/min.}$$

$$\text{M.I.F.R.} = \frac{1}{0.2} \times 60 = 300 \text{ L/min.}$$

(Flow rates to be corrected to B.T.P.S.)

Figure 3



Forced expiratory and inspiratory spirograms in an emphysematous patient (non-miner). Impairment of expiration is much greater than impairment of inspiration.
M.E.F.R. = 35 L/min. M.I.F.R. = 133 L/min.

this study, they are preferred.

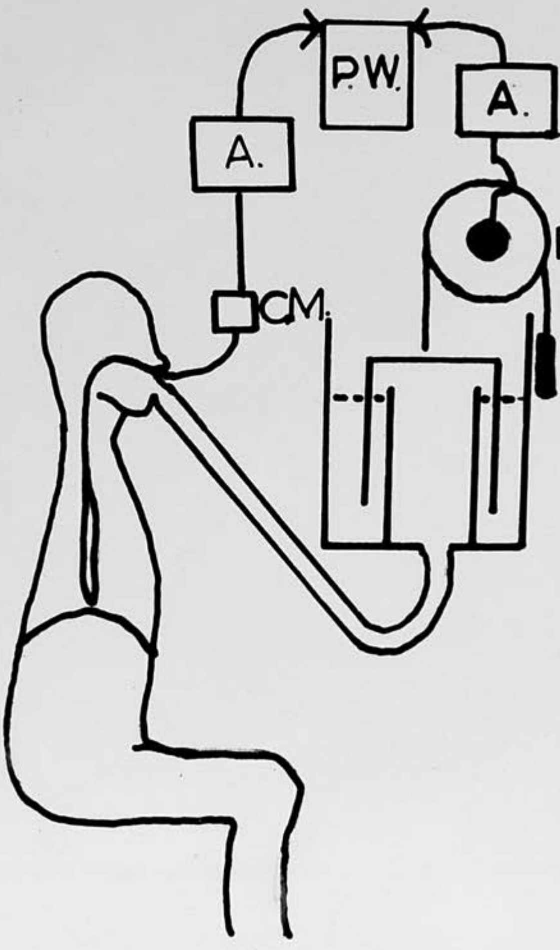
The normal values for M.E.F.R. and M.I.F.R. given by Comroe et al. (1955) are 400-500 litres per minute and they are similar to those found by McNeill et al. (1959).

3. Lung Compliance

This was measured in 34 of the 52 miners. There was no method of selection and the omissions were due simply to lack of time, and, in two instances, to a failure in passing the oesophageal tube.

The subject was in the sitting position and the pressure applied to the lungs during breathing was assumed to be equal to the intraoesophageal pressure. The pressure was recorded through a capacitance manometer either onto a cathode ray oscilloscope or a direct pen and ink writer (Kelvin Hughes double channel recorder). The volumes breathed were recorded electrically by a potentiometer attached to a pulley wheel on a spirometer. The signal was amplified and led to the direct writer or oscilloscope where it was traced immediately above the pressure record. A simultaneous signal applied to the pressure and volume recording systems showed that there was a lag in the volume record of 0.02 seconds. In practice this was ignored. Figure 4 shows the apparatus used.

Figure 4



Method of obtaining simultaneous records of tidal volume and oesophageal (intrathoracic) pressure.
C.M. = capacitance manometer. P = potentiometer.
A = amplifier. P.W. = direct pen writer.

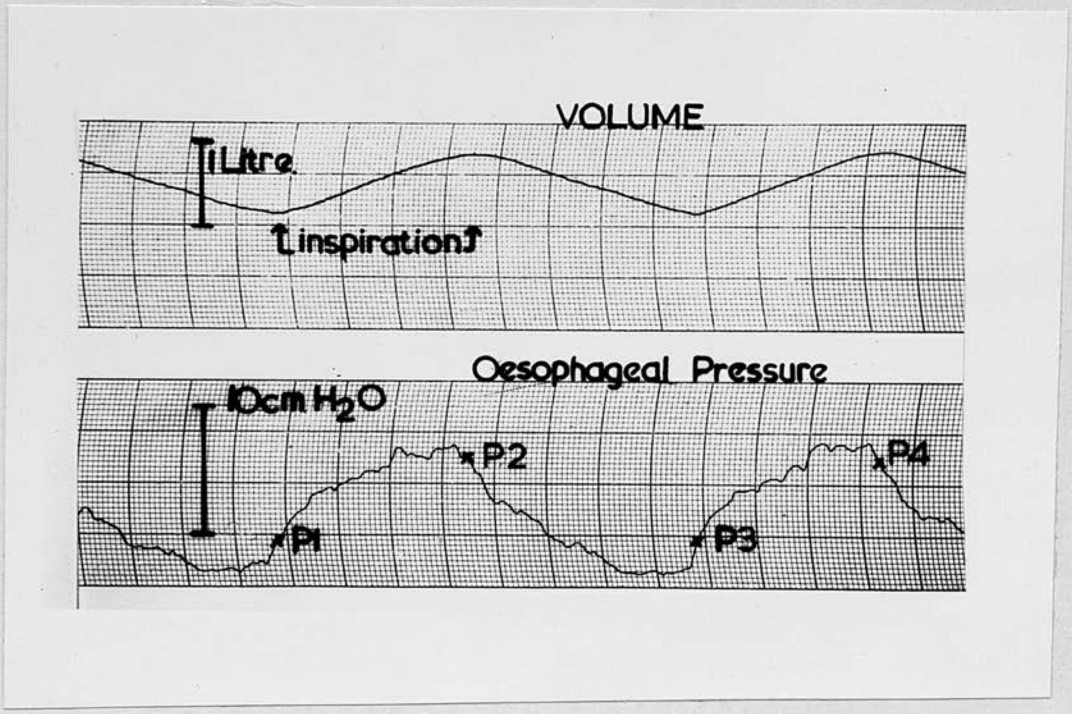
The procedure was to pass an air-filled oesophageal balloon about 10 cm. long into the lower oesophagus. The subject then breathed in and out of the spirometer at a normal resting rate and tidal volume. From the peaks on the volume tracing, the points of "no air flow" were fixed and from the corresponding points on the pressure tracing, the pressure difference required to introduce the volume was calculated. Compliance was then expressed in ml. per cm. H_2O. Figure 5 shows the method of measurement which was done over a minimum of three respiratory cycles. The predicted normal values for compliance are obtained from the equation based on lung volumes by Marshall (1957), compliance (L/cm. H_2O) = 0.05 x F.R.C.

4. The diffusing capacity of the lungs for carbon monoxide (DL_{CO})

As this is the prime measurement in this study the basis of the test used is stated and some technical aspects discussed in detail.

The diffusing capacity of the lungs for any gas is expressed as ml. of gas diffusing per minute per mm. Hg. pressure gradient between the alveolus and the capillary blood. If the CO is the test gas the mean alveolar pressure during the period of diffusion is equal to the

Figure 5



Simultaneous records of tidal volume and oesophageal pressure. Maximum amplitude of pens = 4 cm.
P 1, 2, 3 and 4 = pressure at points of "no air flow".

$$\text{Compliance} = \frac{\text{inspired volume (ml)}}{\text{P1} - \text{P2 (cm } H_2O)}$$

mean pressure gradient as there is no significant back pressure from capillary blood. The greatest error arising from this assumption would be about 8% in the measurement of the DL_{CO} and that would only be in the extreme case of a heavy smoker with 10% COHb in his blood (Ogilvie et al., 1957). The test used was the standardised breath-holding test described in detail by Ogilvie, Forster, Blakemore and Morton (1957). Their technique, which is a modification of the original Krogh method (1915), was followed in almost every detail.

The subject makes a full inspiration from the level of his residual volume, of a gas mixture containing about 21% O_2, 0.3% CO, 10% He and 68.7% N_2. The breath is held for 10 seconds and then rapidly expired. The first 750 ml. are rejected, as this is required to wash out the dead space gas (Fowler, 1949) and then an alveolar sample is collected. For the purpose of gas analysis this sample need only be about 400 ml. and in practice little more was collected so that timing errors and large volume changes during the period of collection could be avoided. The expirate is then analysed for He and CO. The initial concentration of CO in this sample at the start of breath-holding, can be calculated from the dilution of the inspired He as this is an inert, insoluble gas which undergoes dilution only.

Thus,

$$\text{Initial CO conc. in expired alveolar sample} = \frac{\text{(He conc. in expired alveolar sample)}}{\text{(Inspired He conc.)}} \times \text{Inspired CO conc.}$$

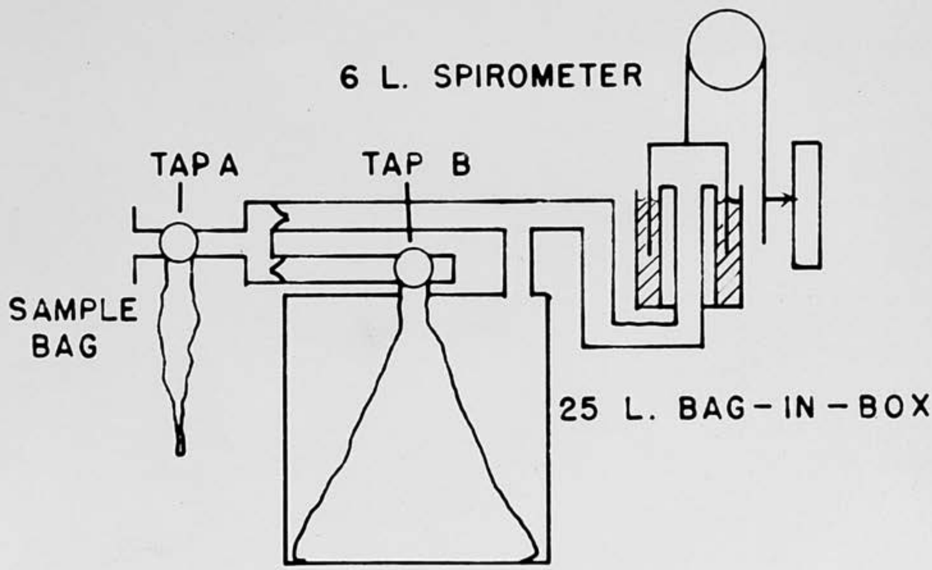
From the knowledge of this, and the final CO conc. in the alveolar sample, and knowing the exact breath-holding time, the DL_{CO} may be calculated according to the Krogh equation:-

$$DL_{CO} \left(\frac{\text{ml. CO. S.T.P.D.}}{\text{min. x mm. Hg. CO. tension}}\right) = \frac{\text{Alveolar volume (S.T.P.D.)} \times 60}{\text{Time in seconds of breath-holding} \times \text{(barometric pressure - 47)}}$$

$$\times \text{ natural log } \left(\frac{\text{Initial alveolar CO conc.}}{\text{Final alveolar CO conc.}}\right)$$

The apparatus is shown in Figure 6. Essentially it consists of a circuit linking a Donald-Christie box containing the bag with the special gas mixture, with a spirometer which records volume changes with inspiration and expiration. The subject joins the circuit at the mouth piece, expires down to residual volume and then makes a full and rapid inspiration of the special gas mixture. After breath-holding and during expiration the alveolar sample is taken by turning the tap near the mouth to the collecting bag. The dead space from the mouth piece to the collecting bag is 45 ml. A specimen of the tracing recorded on the

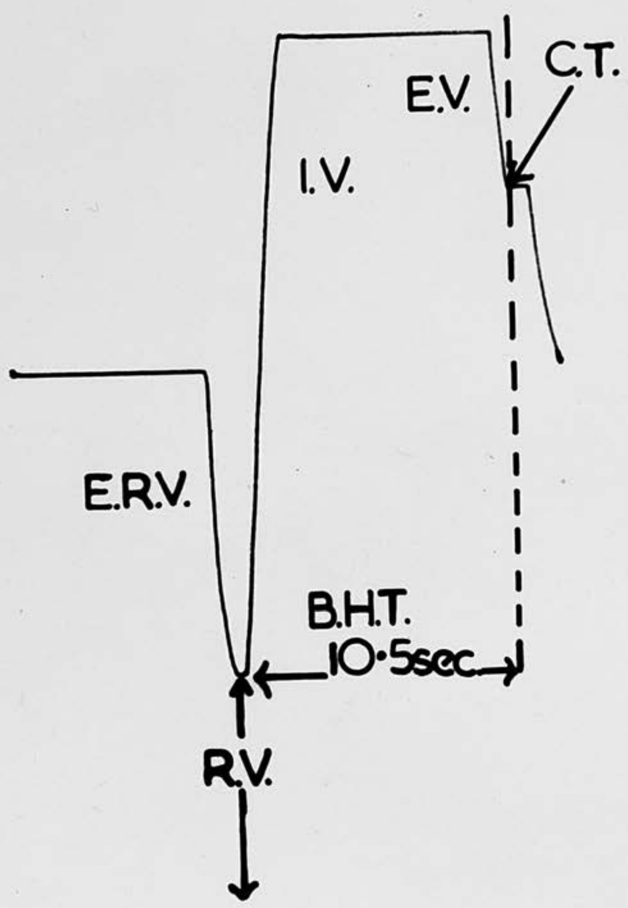
Figure 6



Apparatus used in measurement of diffusing capacity by single breath method.

Special gas mixture for inspiration in 25 litre bag.

Figure 7



Specimen spirometer tracing during measurement of DL_{CO}.

Inspired volume (I.V.) + Residual volume (R.V.) = alveolar volume.

Expired volume (E.V.) exceeds 750 ml.

B.H.T. = breath-holding time.
C.T. = sample collection time.

spirometer is shown in Figure 7. The alveolar volume is obtained by adding the inspired volume to the residual volume previously measured. The diffusion time is measured from the start of inspiration to the start of sample collection. If the time taken to deliver this sample is long, the true diffusion time will be longer than the measured period and this results in an overestimate of DL_{CO}. However, Ogilvie et al. (1957) have shown that if the collection period does not exceed two to three seconds this is not extremely critical although it may result in a 10% overestimate of DL_{CO}. In practice, every effort was made to restrict this period and if only 400-500 ml. are collected the time is well below two seconds in all but the few patients with severe impairment of expiratory flow rates (Ind. M.B.C. below 50% of predicted value in only three of 52 subjects). As the measurement of breath-holding starts with the beginning of inspiration the subject is credited with a longer period than is strictly true for the whole of the inspired volume. This error tends to underestimate the DL_{CO} and to cancel out the error due to the collecting period.

<u>Measurement of CO</u>. This was done by a standard infra-red gas analyser supplied by The Infra Red Development Co. The display is by a meter with two scales of equal length,

0-0.07% CO and 0.05-0.4% CO. Concentrations can be measured to 2% of full scale reading. Standardisation of the instrument was always done before use and was by gas mixtures containing CO in nitrogen supplied by the Company for this purpose.

The instrument is sensitive to water vapour and, therefore, the gas sample was dried by passing it through magnesium perchlorate beforehand. The drying and analysis tubes could be completely flushed by 250 ml. of gas if the dead space of the drying tube and connecting rubber tubing were kept to a minimum.

Because of a compensating chamber containing 100% CO_2 in series with both the analysis and reference tubes, the CO reading was very little affected by the presence of CO_2 in the sample. Repeated tests showed a deflection from 4% CO_2 equivalent to 0.0005-0.001% CO. Because of this, no correction was made for the presence of CO_2 in the alveolar sample.

Measurement of He. This was done on the katharometer already described. As CO_2 gives a negative deflection on this instrument the alveolar sample was passed through soda lime before measurement. This, however, shrinks the total gas volume and, so, falsely concentrates the He. A reduction to 96% of the value is made on the assumption that about 4% CO_2 is present in the alveolar sample. This is lower than the value of 5.6% CO_2 usually given for alveolar gas because of the dilution of alveolar CO_2 that occurs when a full inspiration is made from residual volume. Under these circumstances, even after a 10 sec. breath-holding period, the values are about 4% (DuBois, 1952; Rankin, McNeill, Forster, unpublished observations, 1956).

<u>Number of estimations</u>. Three estimates each were done on 51 of the 52 miners. There was a three to five minute interval between tests. A result was only rejected if there was an obvious technical error at the time. The coefficient of variation of the tests in the same subject is discussed later.

<u>Normal values</u> are based on a regression equation for DL_{CO} and size given by Ogilvie et al. (1957),

$$DL_{CO} = \text{surface area } (M^2) \times 18.85 - 6.8.$$

A discussion of the effect of age will follow later.

RESULTS

The results presented in this section are obtained from an analysis of the data shown in Tables I, II, III, IV and V in the appendix.

The plan has been to relate the results of the physiological tests to age, X-ray category, the presence or absence of chronic bronchitis, smoking habits and dyspnoea grade of each subject. The frequency and distribution of these variables in relation to each other is shown in Table VI.

The subjects fall into two broad groups according to their source. Group 1 is made up of 16 miners from the Fitness Centre at Bridge of Earn and 10 working miners selected at random from the records of the National Coal Board. None of the miners from the Fitness Centre was there on account of a respiratory disability. Group 2 is made up of 20 miners from the Industrial Chest Diseases Unit at Bridge of Earn Hospital and 4 from Glenlomond Hospital and all were in hospital for an assessment of their pneumoconiosis.

The composition of both Groups in respect of age and X-ray category is seen in Tables VII and VIII.

TABLE VI

	Age			X-ray category					Chronic bronchitis		Smoking habits				Dyspnoea grade			
	-49	50+	60+	1	2	3	A	B+	Absent	Present	OS	S1	S2/3	ES	1	2	3	4/5
Age																		
-49	8			5	1	-	2	-	7	1	-	-	8	-	2	5	1	-
50+		25		9	6	2	6	2	10	15	4	6	12	3	3	10	10	2
60+			19	3	6	2	3	5	11	8	3	6	8	2	2	8	8	1
X-ray																		
1	5	9	3	17					10	7	1	2	10	4	3	9	3	2
2	1	6	6		13				9	4	5	2	6	-	4	5	4	-
3	-	2	2			4			2	2	1	1	2	-	-	2	2	-
A	2	6	3				11		5	6	-	3	8	-	-	6	5	-
B+	-	2	5					7	2	5	-	4	2	1	-	1	5	1
Chronic bronchitis																		
-	7	10	11	10	9	2	5	2	28		6	3	16	3	6	13	8	1
+	1	15	8	7	4	2	6	5		24	1	9	12	2	1	10	11	2
Smoking																		
OS	-	4	3	1	5	1	-	-	6	1	7				2	3	2	-
S1	-	6	6	2	2	1	3	4	3	9		12			-	3	7	2
S2/3	8	12	8	10	6	2	8	2	16	12			28		5	15	7	1
ES	-	3	2	4	-	-	-	1	3	2				5	-	2	3	-
Dyspnoea																		
1	2	3	2	3	4	-	-	-	6	1	2	-	5	-	7			
2	5	10	8	9	5	2	6	1	13	10	3	3	15	2		23		
3	1	10	8	3	4	2	5	5	8	11	2	7	7	3			19	
4/5	-	2	1	2	-	-	-	1	1	2	-	2	1	-				3

The 3 age groups used are 49 and under, 50 to 59 and 60 and over.
X-ray categories as explained in text. Category B+ includes complicated pneumoconiosis of category B or more.
Under smoking habits, subgroups 2 and 3 are combined.
Under dyspnoea, grades 4 and 5 are combined.

TABLE VII

Group 1. Subjects from Fitness Centre and Home

Age group	X-ray category 1	2	3	A	B+	Total
49-	2	1	-	1	-	4
50+	5	2	1	2	1	11
60+	2	4	2	2	1	11
Total	9	7	3	5	2	26

TABLE VIII

Group 2. Subjects from I.C.D.U. and Glenlomond

Age group	X-ray category 1	2	3	A	B+	Total
49-	3	-	-	1	-	4
50+	4	4	1	4	1	14
60+	1	2	-	1	4	8
Total	8	6	1	6	5	26

Although Group 2 includes a few more miners with complicated pneumoconiosis than Group 1, the overall distribution of age and X-ray category is similar.

When age, dyspnoea grade and the presence or absence of chronic bronchitis are considered the similarity of both groups is again apparent.

TABLE IX

	Average Age	Average Dyspnoea Grade	Chronic Bronchitis -	+
Group 1 (26 miners)	56.5	2.19	15	11
Group 2 (26 miners)	56.7	2.57	13	13

The average dyspnoea grade in Group 2 is worse than Group 1 but the difference is not statistically significant (Chi squared = 4.38, $P > 0.3$).

An important question, however, is whether in the actual objective measurements of pulmonary function Group 2 is significantly different from Group 1, thus producing a bias in the results.

To test this the Ind. M.B.C., chosen as the main test of ventilatory function, and DL_{CO} as the main test of the investigation, have been compared in each group.

TABLE X

	Mean Ind. M.B.C. L/min	Mean DL_{CO} ml/min/mmHg
Group 1	90.4	21.6
Group 2	91.7	23.9

The mean values for Group 2 for both tests are actually higher than Group 1 but the differences are not significant (difference in means of DL_{CO} = 2.3, standard error = 2.12, t = 1.08 which is not significant).

The conclusion is that although Group 2 is slightly worse in respect of X-ray category and dyspnoea grade, there is no adverse effect in respect of ventilatory capacity and diffusion. Both groups are therefore considered together and account is taken of the variables for each individual as shown in consolidated form in Table VI.

The results of the physiological tests are presented under the following headings:-

1. Diffusing capacity of the lungs for carbon monoxide.
2. Ventilatory function.
3. Lung volumes.
4. Lung compliance.
5. Blood findings.

A summary of the results with a table indicating significant differences, follows this and finally the inter-relationship between tests is examined.

1. Diffusing capacity of the lungs for carbon monoxide (DL_{CO})

This was measured in 51 miners and the mean result of 3 estimations on each individual is used in the analysis.

The mean DL_{CO} for all miners is 22.74 ml/min/mmHg and the standard deviation is 7.2. The standard deviation of the 3 estimations on the same individual is 1.67 and the coefficient of variation is 7.3%.

Expressed as a percentage of the predicted normal value (Ogilvie et al., 1957) the mean DL_{CO} for all is 85.6% and the standard deviation 24.9%. For the purposes of correlation between different tests a value has been estimated for the one miner in whom the test was not done. This value takes into account his age and X-ray category; it is not included in the degrees of freedom in the calculations.

The variables of age, X-ray category, chronic bronchitis, smoking habits and dyspnoea grade are considered in turn for each test of lung function.

Age. The three separate age groups shown in Table VI are used and the mean value of DL_{CO} in each is,

49 and under (8)	=	26.8 ml/min/mmHg
50 to 59 (25)	=	23.8 " "
60 and over (19)	=	19.6 " "

The reduction in mean value with age is significant (variance ratio $F = 3.8$, $P < 0.05$).

If DL_{CO} is expressed as a percentage of the predicted normal value which is calculated on the basis of the subject's surface area, the relationship to age persists.

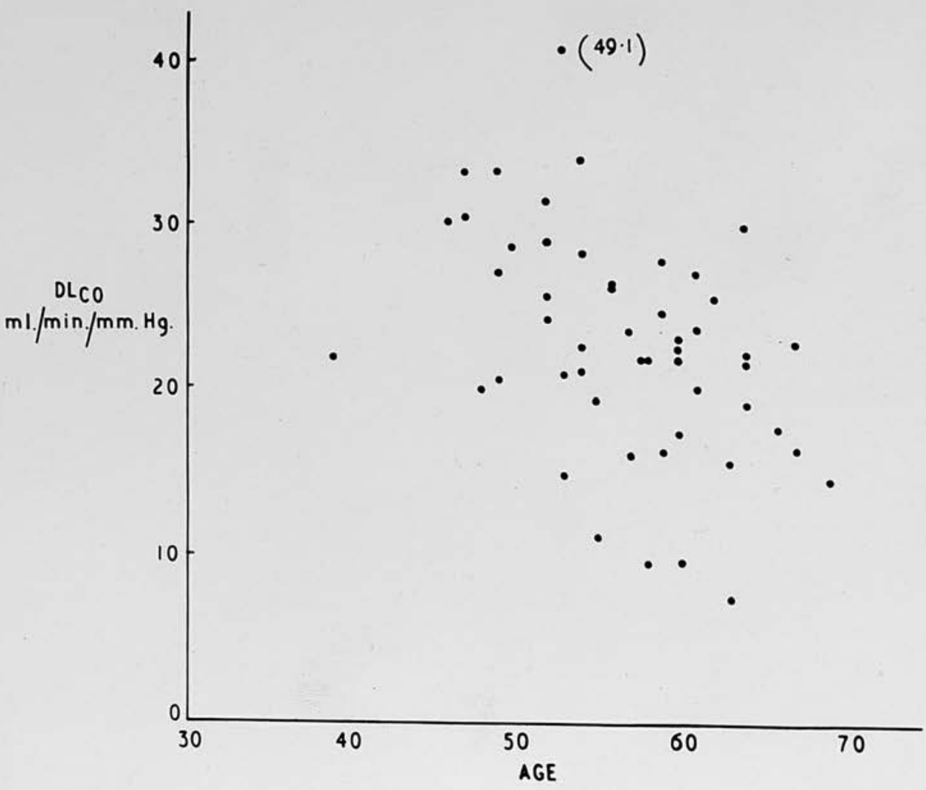
Figure 8 shows the general relationship between DL_{CO} and age in this study.

X-ray category. There are five X-ray groups in Table VI and the fifth contains all miners with complicated pneumoconiosis of Category B or more. The mean values for DL_{CO} are,

Category	1	(17)	=	26.1	ml/min/mmHg	
"	2	(13)	=	24.1	"	"
"	3	(4)	=	15.5	"	"
"	A	(11)	=	23.1	"	"
"	B+	(7)	=	15.9	"	"

The difference between the categories is significant ($F = 4.7$, $P < 0.01$) but the trend with radiological progression of the disease is irregular. Thus Category A has a higher mean value than might be expected and this feature is seen in some of the other tests of lung function as well. If Category A is examined in respect of the background of simple pneumoconiosis in each subject, there

Figure 8



is a significant difference ($P < 0.01$) between the means for the 6 miners in category 2A (DL_{CO} = 26.3) and the five miners in category 3A (DL_{CO} = 19.3). However, those in category 3A have an average age of 60 years and those in category 2A an average age of 54 years, and this can account for part of the difference. The residual difference nevertheless is still significant (difference in means = 7.0, difference attributed to age = 2.5, residual difference = 4.5, standard error of difference = 1.77, $P < 0.05$).

Table XI gives the mean values of DL_{CO} in each X-ray category for each age group.

TABLE XI

Mean DL_{CO} in different age groups and X-ray categories

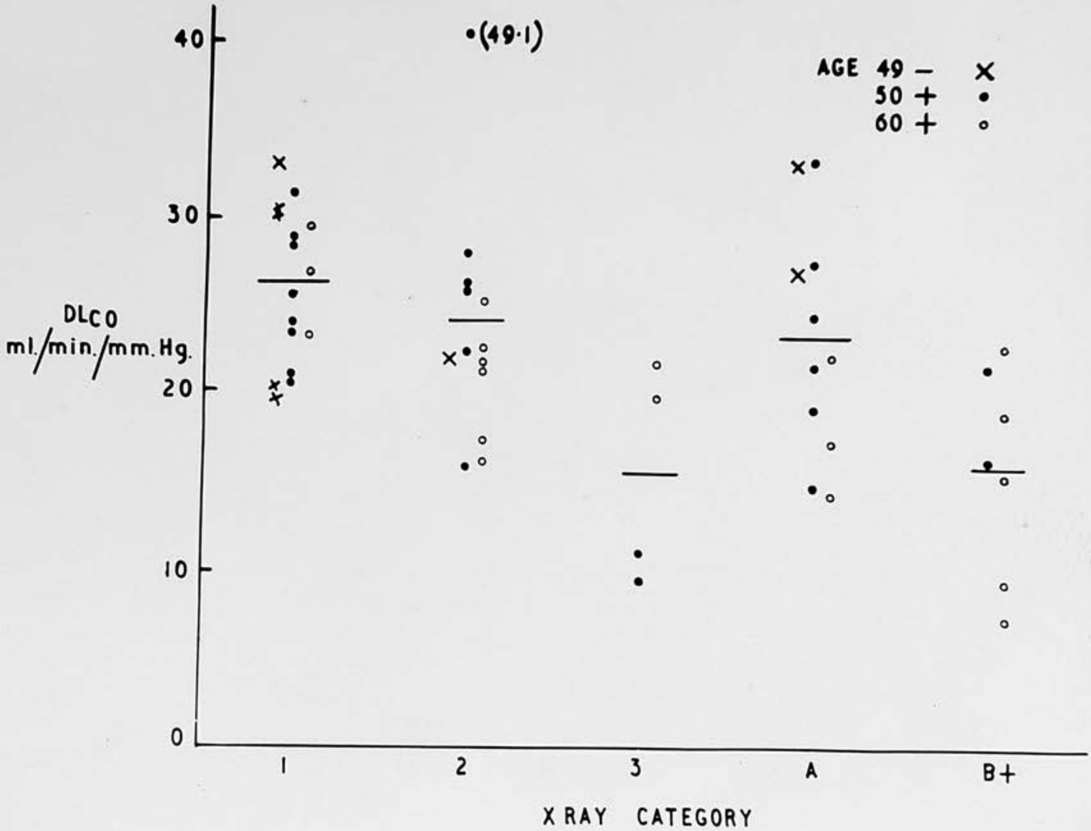
Age group	X-ray category 1	2	3	A	B+
60+	26.4 (3)	20.7 (6)	20.7 (2)	17.5 (3)	14.7 (5)
50 to 59	25.6 (9)	27.8 (6)	10.2 (2)	23.4 (6)	18.8 (2)
49-	26.6 (5)	21.8 (1)	-	29.9 (2)	-

Numbers within groups in parenthesis.

Figure 9 shows the relationship between DL_{CO} and X-ray category with age groups indicated.

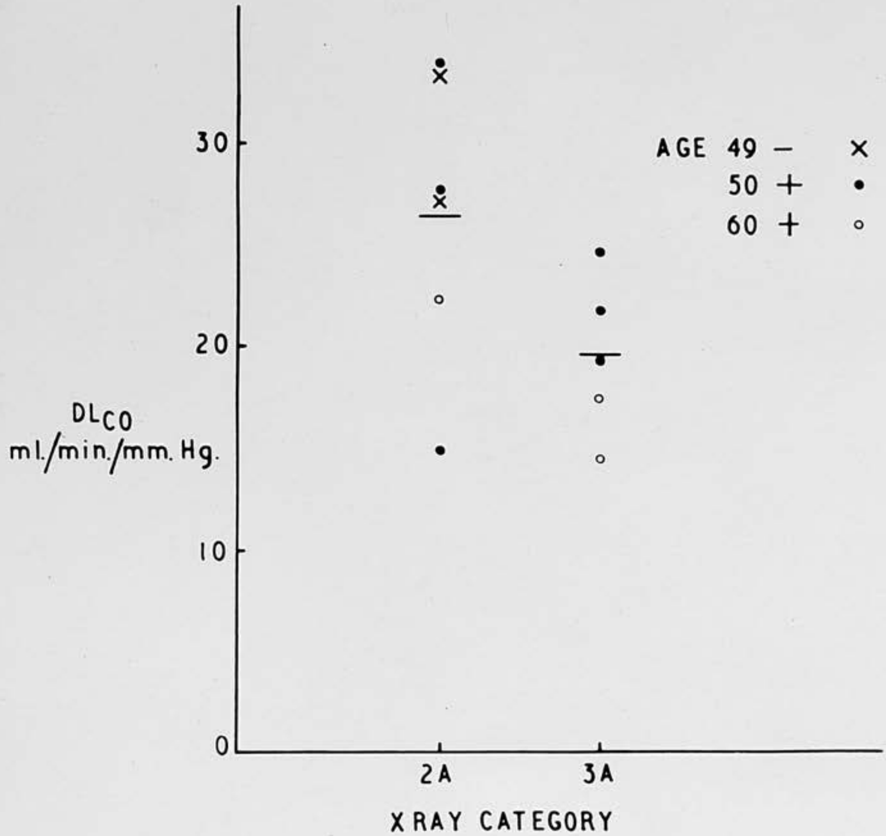
Figure 10 shows DL_{CO} in X-ray categories 2A and 3A with age groups indicated.

Figure 9



•(49·1)
AGE 49 − ×
50 + •
60 + ∘
DLCO
ml./min./mm.Hg.
40
30
20
10
0
1
2
3
A
B+
X RAY CATEGORY

Figure 10



Chronic bronchitis. No significant difference has been demonstrated between the mean DL_{CO} values for those with and without chronic bronchitis.

Without chronic bronchitis (28) = 24.3 ml/min/mmHg

With chronic bronchitis (24) = 21.0 ml/min/mmHg

Although the difference between the means is not significant it is suggestive, but the bronchitics were also older and had slightly worse X-ray categories.

Smoking habits. No significant differences have been found between the mean values for DL_{CO} in the different smoking groups.

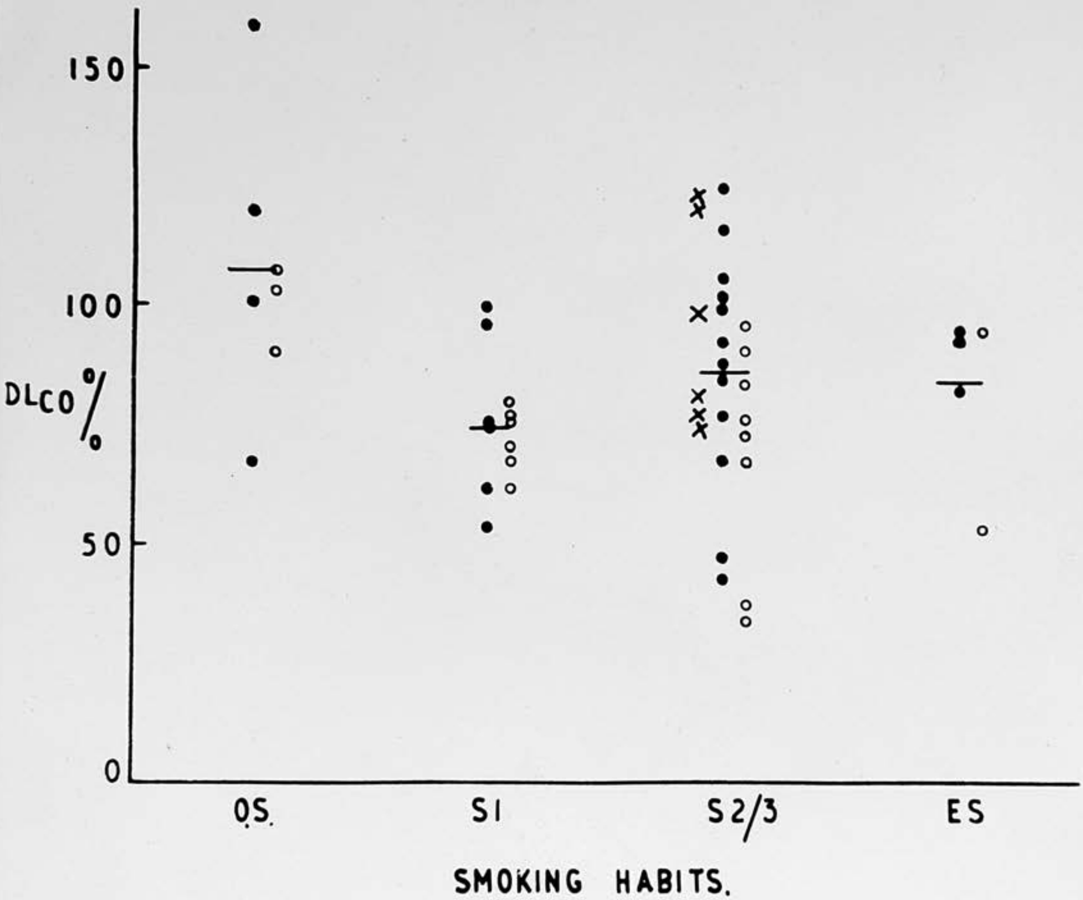
O.S. (non-smokers, 7)	= 27.8 ml/min/mmHg
S 1 (1-69 G/week, 12)	= 19.8 " "
S 2/3 (over 69 G/week, 28)	= 22.4 " "
E.S. (ex-smokers, 5)	= 24.6 " "

There is a difference in the mean values between smokers and non-smokers generally, but there is no consistent trend within the smoking grades.

If DL_{CO} is expressed as a percentage of the normal value which corrects for individual size, the differences between the groups becomes significant ($F = 2.99$, $P < 0.05$) but there is still no obvious trend. This may be because all the miners in the youngest age group were in group S 2/3.

Figure 11 shows the relationship between the diffusing capacity and smoking.

Figure 11



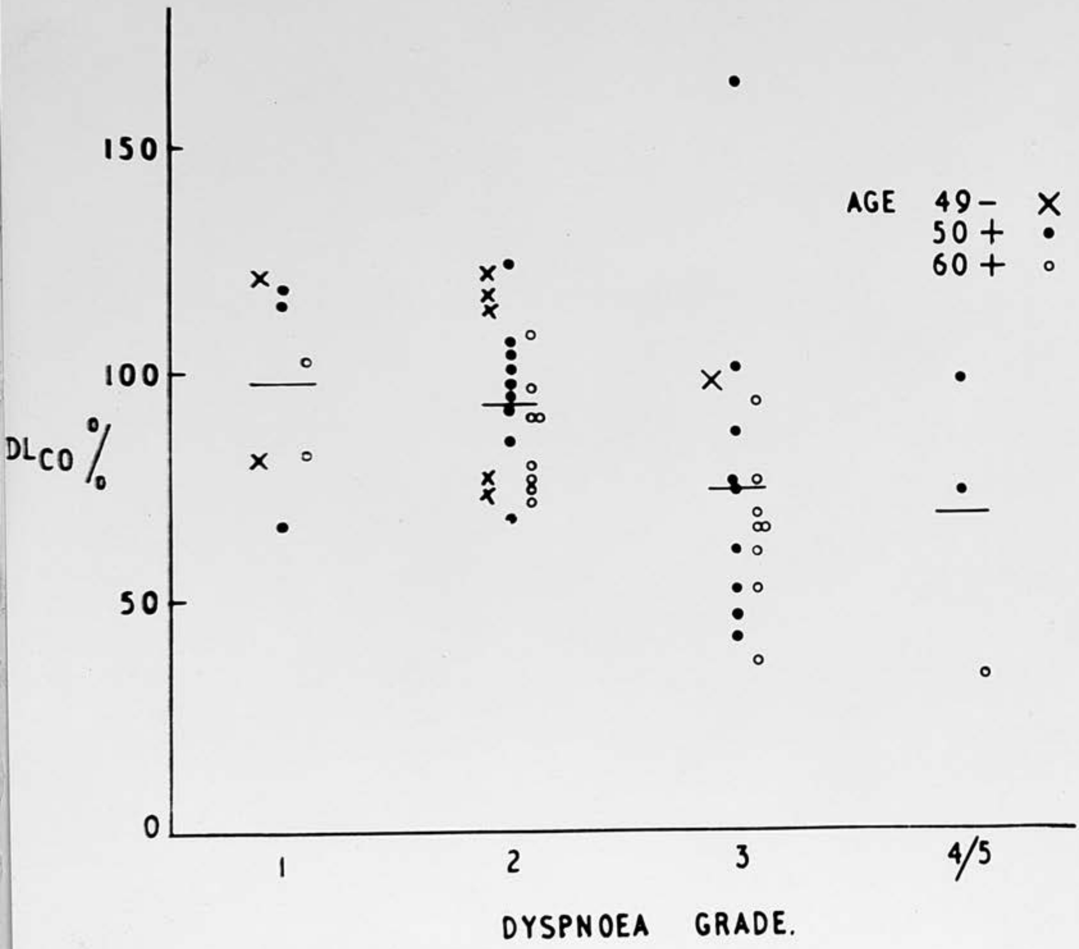
Dyspnoea. As indicated in Table VI, dyspnoea grades 4 and 5 have been combined. The mean values for DL_{CO} in the different grades are,

Dyspnoea grade 1	(7)	= 26.4	ml/min/mmHg
" " 2	(23)	= 24.1	" "
" " 3	(19)	= 20.5	" "
" " 4/5	(3)	= 18.9	" "

Although the difference between the grades is suggestive it does not quite reach significant levels. If DL_{CO} is expressed as a percentage of the predicted value which takes surface area into account, the differences become significant ($F = 2.99$, $P < 0.05$).

Figure 12 shows the relationship between DL_{CO} and dyspnoea and indicates the age groups.

Figure 12



Since there are significant differences in DL_{CO} for the different X-ray categories, it is of interest to see the relationship between DL_{CO} and dyspnoea within the X-ray categories.

TABLE XII

Mean DL_{CO} in Dyspnoea grades and X-ray Categories

X-ray category	Dyspnoea grade 1	2	3	4/5
1	30.2 (3)	25.2 (9)	25.3 (3)	24.7 (2)
2	23.6 (4)	21.9 (5)	27.1 (4)	-
3	-	20.7 (2)	10.2 (2)	-
A	-	25.4 (6)	20.3 (5)	-
B+	-	21.5 (1)	16.5 (5)	7.3 (1)

Numbers within groups are in parenthesis.

Relationship of the diffusing capacity of the lungs to other factors

(i) Cardiac disease. There was no evidence, on physical examination, of cardiac failure in any subject at the time of study.

An E.C.G. record was obtained in 44 of the 52 miners. There was no significant abnormality in 35 of these although a vertical heart pattern was seen in 14 and a P pulmonale wave in 1. The abnormalities noted in the other 9 are seen in Table XIII. The ages, DL_{CO} values, and X-ray categories are also given and it is obvious that there is no difference between the 9 with E.C.G. abnormalities and the remainder in respect of either age or diffusion.

TABLE XIII

E.C.G. Abnormalities

Name	Age	E.C.G.	DL_{CO} ml/min/mmHg	% normal DL_{CO}	X-ray category
R.S.	46	Anteroseptal infarct	30.0	121	1--/-
J.H.	50	Anteroseptal infarct	28.3	93	1--/-
W.A.	54	Anteroseptal infarct	22.2	67	2--/-
R.B.	54	Myocardial ischaemia	20.8	74	1--/-
J.S.	55	Posterior infarct	11.0	47	3--/-
W.M.	56	Low voltage flat T waves (myxoedema)	25.9	101	2--/-
T.W.	64	Right bundle branch block	21.7	96	2--/-
J.C.	64	Myocardial ischaemia	18.9	70	2B2/1
D.M.	67	Right ventricular hypertrophy	22.5	83	2--/-
Mean of group	56.7		22.4	83.6	
Mean of remainder	56.6		22.8	86.0	

(ii) Industrial history. There is an obvious correlation between the age of the miner and the length of time he has spent in the mines. As a relationship has already been demonstrated between DL_{CO}, age and X-ray category, the separate effect of years spent in the mines is difficult to demonstrate.

However, if attention is paid to years spent, as specified by the miner, either exclusively or predominantly on stone-work within the mines a relationship to the diffusing capacity is seen. Table XIV lists the 8 miners who have spent 10 or more years on stone-work and gives details of their age, X-ray category, DL_{CO} and Ind. M.B.C. A significant difference exists between these men and the remainder in respect of DL_{CO} but not Ind. M.B.C. (difference in mean DL_{CO} = 6.9, standard error of difference = 2.78, $t = 2.46$, $P < 0.02$). However, those who had spent 10 or more years on stone-work were slightly older on average than the others, and this may have accounted for part of the difference.

No correction has been made for X-ray category because it is considered that stone dust would influence this also.

TABLE XIV

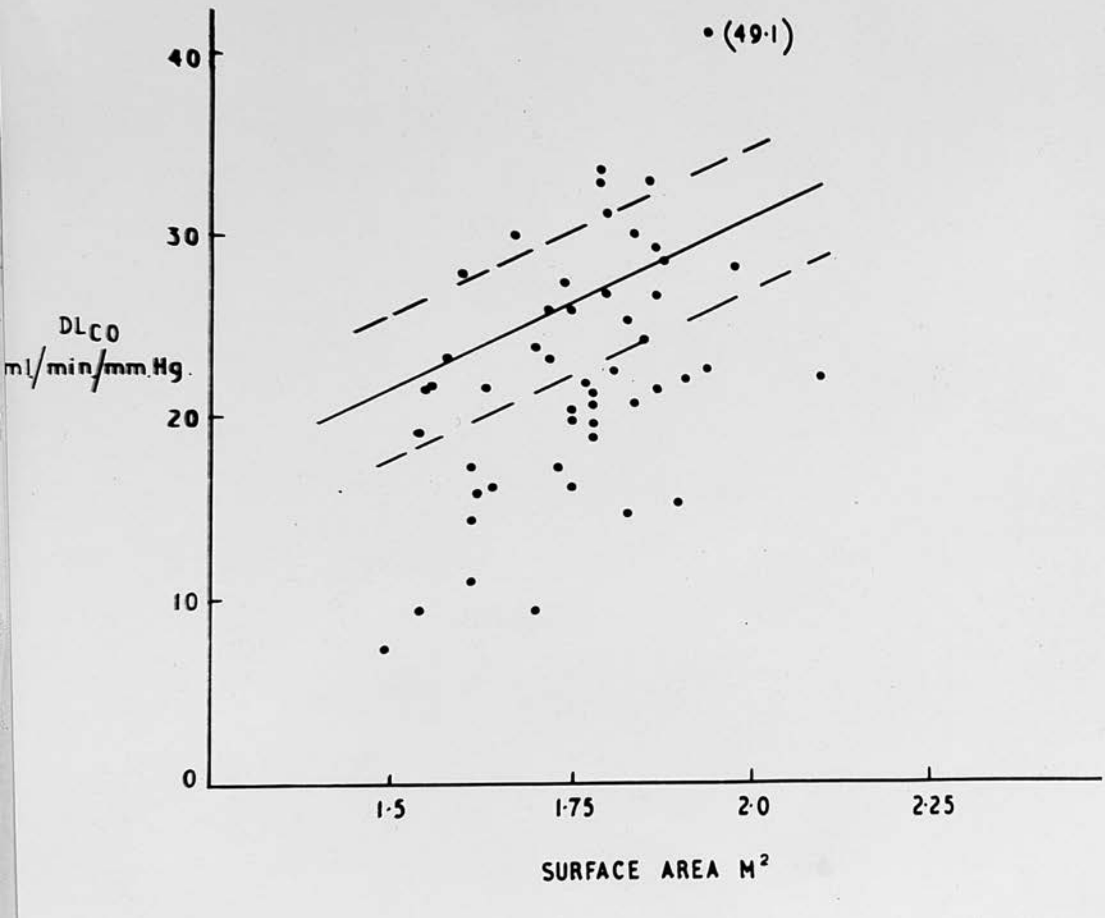
Ten or more years stone-work in mines

Name	Age	Total yrs. in mines	Yrs. on stone-work	X-ray category	DL_{CO} ml/min/mmHg	Ind. M.B.C. L/min
J.H.	52	38	10	1--/-	25.4	105
J.S.	55	39	24	3--/-	11.0	105
W.M.	58	44	18	3A1/-	21.5	85
J.J.	59	31	15	3C4/4	16.1	63
E.L.	60	45	17	2A1/-	22.1	59
D.M.	63	44	16	3D4/3	7.3	50
C.P.	63	43	16	2C2/2	15.3	90
T.C.	67	46	12	2--/-	16.1	87
Mean	59.7	41.2	16.0	-	16.8	80.5
Mean of others	56.0	38.8	1.25	-	23.7	93.0
			S.D. (all miners)		7.2	30.7
			S.E. of difference		2.78	11.8

Comparison of DL_{CO} results with predicted normal values

Ogilvie, Forster, Blakemore and Morton (1957) considered that the regression of DL_{CO} on surface area was linear and that the best equation for predicting results in normals was, $DL_{CO} = 18.85 \times S.A. - 6.8$. For several reasons this cannot be accepted unreservedly as the best yardstick for the subjects in this study. Their equation is based on the results obtained in 28 normal subjects including males and females, and there were, in fact, only 5 males in the 40 to 70 year age group. Nevertheless, it is important to compare results because the methods used in both studies are identical. Variations in the lung volume at which the measurement of DL_{CO} is made, have contributed to a wide scatter in the published normal values (Forster, 1957; McGrath and Thomson, 1959). Figure 13 shows the results obtained in miners with pneumoconiosis in this study, plotted against surface area and compared with the regression line for normals given by Ogilvie et al. The standard deviation of their estimate is also shown and it can be seen that 25 of the 51 miners fall below one standard deviation instead of a possible 9, had they all been normal.

Figure 13



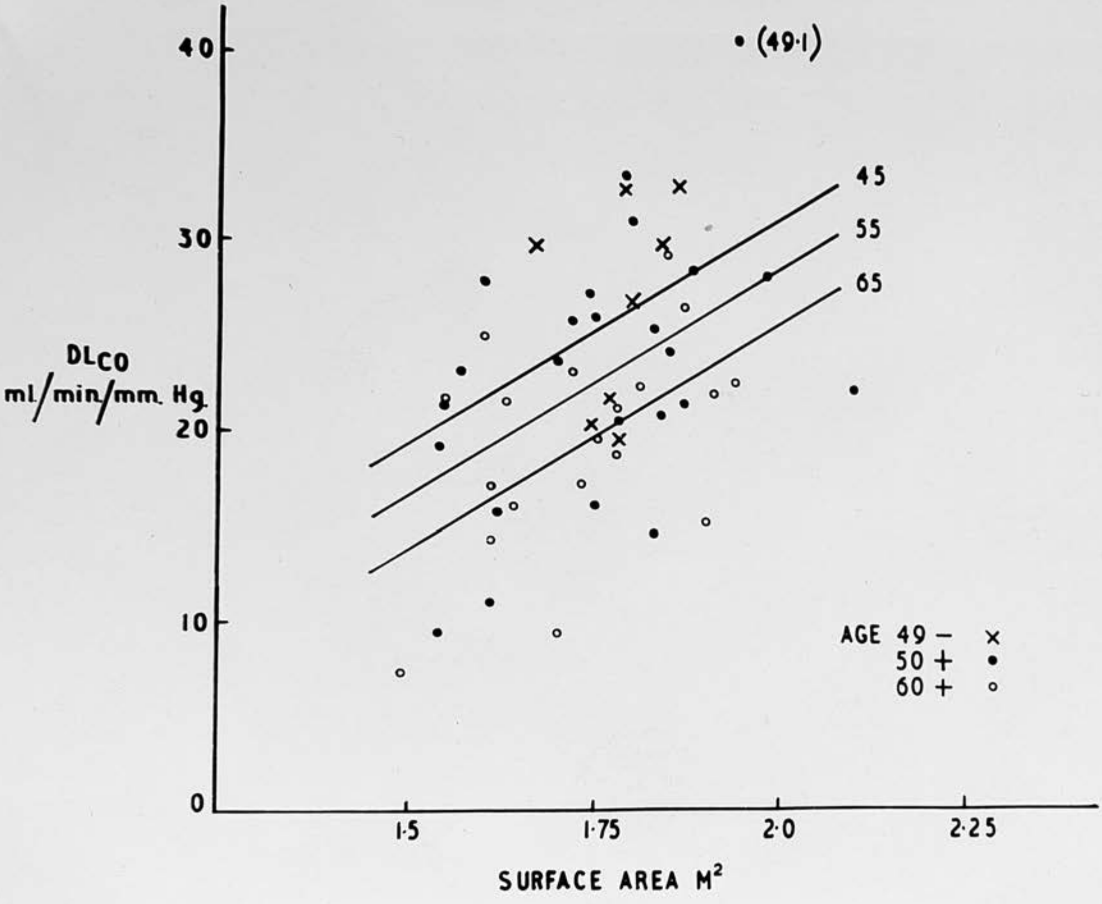
DL_{CO} plotted against surface area.
Regression line (and standard deviation) for normals from Ogilvie et al., 1957.

Forster (1957) reviewed the effect of age on DL_{CO} and found the evidence inconclusive. Cohn, Carroll, Armstrong, Shephard and Riley (1954) reported a significant relationship between age and the maximal diffusing capacity of the lungs for oxygen, but this may have been due to a limit in cardiac output rather than the diffusing capacity. More recently, Donevan, Palmer, Varvis and Bates (1959) have reported a relationship between DL_{CO} and age measured by the steady state method and McGrath and Thomson (1959) found a similar relationship using the single breath technique.

In 39 normal males, McGrath and Thomson found that the best equation for predicting results was a multiple regression between age and surface area. The equation is, $DL_{CO} = 0.29 \times \text{age} + 24 \times \text{S.A.} - 3.4$. The number they had in the 40 to 70 year age group was only 16 but the evidence did favour a relationship to age and is in keeping with the results obtained in this study. There is one detail, however, in which the estimation of DL_{CO} by McGrath and Thomson differs from that used in this study. The alveolar volume during breath-holding was calculated from the dilution of helium on a single breath, whereas here it is calculated from the addition of the inspired volume to the residual volume measured previously by a multiple breath technique. The latter method gives a higher volume when there is a mixing defect in the lung, and since the alveolar volume appears in the numerator of the equation for calculating DL_{CO} the results may be relatively higher in abnormals.

Figure 14 shows the results obtained in the miners plotted against surface area and compared with the regression lines of McGrath and Thomson for those of 65, 55 and 45 years of age. The symbols indicate the age groups of the miners. Twenty-four of the 51 are actually below the predicted value but there is a coefficient of variation about the regression lines of 18% and if only those below this are counted the number falls to 10. Of the 27 who do better than the predicted value, 15 score more than 118% whereas if all the subjects had been normal this might have occurred in 9. This is illogical because, whereas there are reasons for expecting low values, there are none for supposing that miners with pneumoconiosis should do better than normal, particularly when both body size and age are taken into account. The conclusion is that the regression equation of McGrath and Thomson is unsuitable for the purposes of this study, despite the cognisance it takes of size and age, and the probable reason for this is the different method used in calculating alveolar volume which gives a relative boost to the results of the miners.

Figure 14



DL_{CO} plotted against surface area and age groups indicated.
Regression lines for normals of 45, 55 and 65 years from McGrath and Thomson, 1959.

2. Ventilatory Function

(i) Indirect maximum breathing capacity (Ind. M.B.C.)

This was measured in all subjects and in each, the best of 3 measurements was accepted. The mean Ind. M.B.C. for all subjects is 91.1 L/min and the standard deviation is 30.7 L/min.

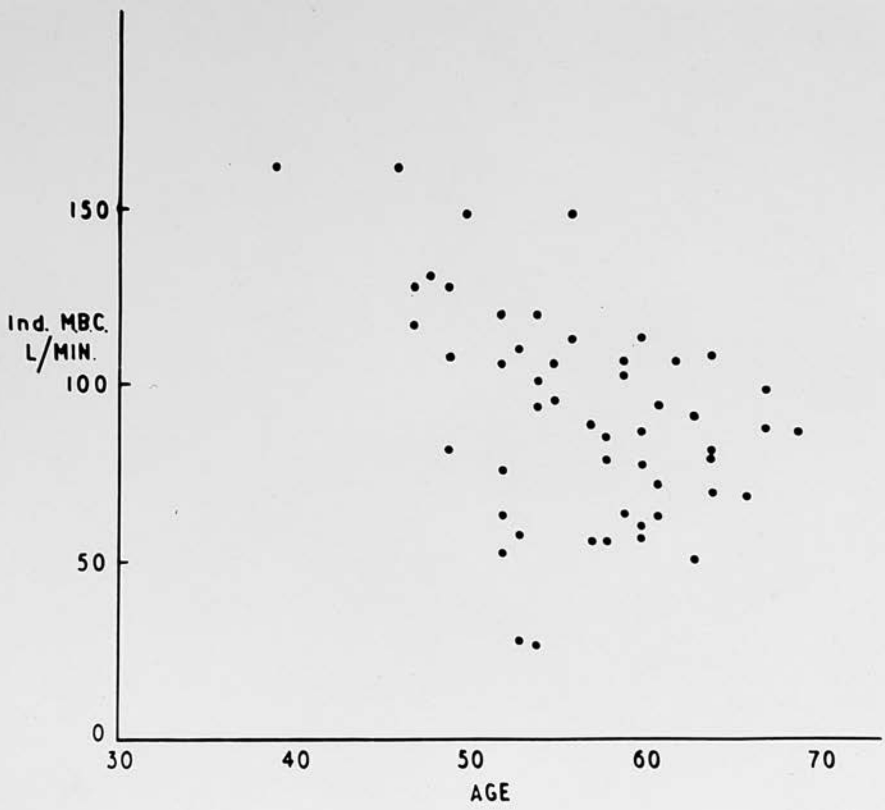
Expressed as a percentage of the predicted normal value, the mean Ind. M.B.C. is 85.8% and the standard deviation is 25.3%.

Age. As in normals, a highly significant relationship has been found between Ind. M.B.C. and age ($F = 8.4$, $P < 0.01$). The mean values for the age groups are,

49 and under (8) = 126 L/min
50 to 59 (25) = 87 L/min
60 and over (19) = 81 L/min

If Ind. M.B.C. is expressed as a percentage of the predicted value which is based on age, the relationship is no longer apparent. Figure 15 shows the relationship of Ind. M.B.C. to the age of the miners in this study.

Figure 15



X-ray category. There is no significant difference between the mean Ind. M.B.C. values in the X-ray categories. The mean values decrease slightly with radiological progression of the disease but the scatter within the categories is large.

Category	1	(17)	=	97 L/min
"	2	(13)	=	96 L/min
"	3	(4)	=	91 L/min
"	A	(11)	=	89 L/min
"	B+	(7)	=	71 L/min

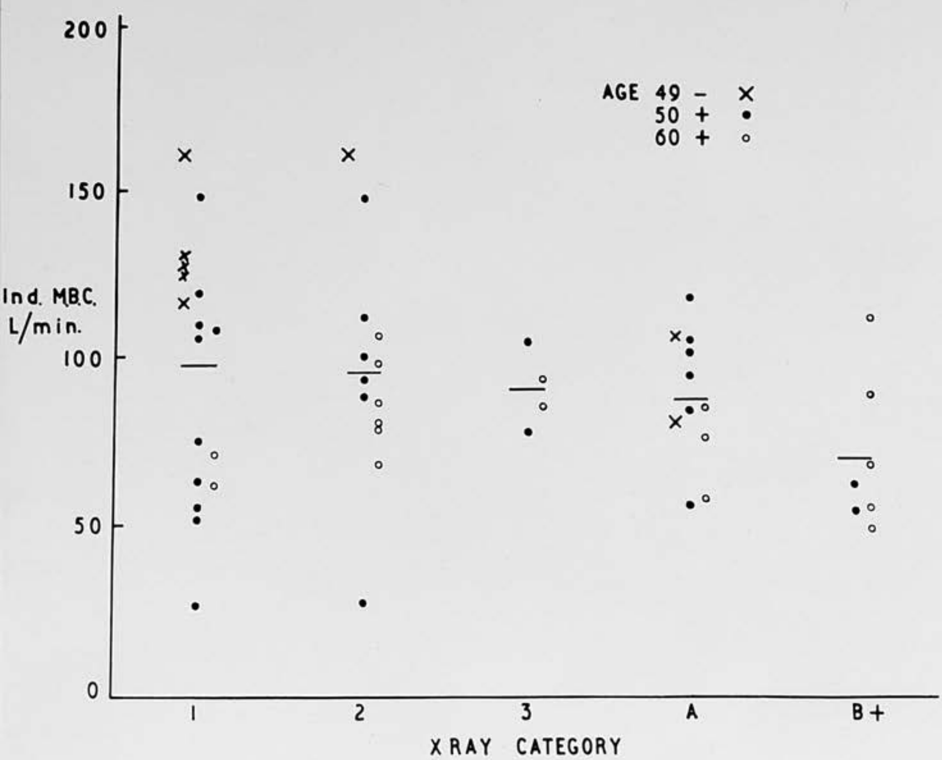
Figure 16 shows the relationship and indicates the age groups.

Chronic bronchitis. No significant difference has been demonstrated between the mean Ind. M.B.C. of those with and without chronic bronchitis. Those without chronic bronchitis do better and the difference is suggestive, but does not reach significant levels ($F = 3.28$, $0.2 > P > 0.05$).

Without chronic bronchitis (28) = 98 L/min

With chronic bronchitis (24) = 83 L/min

Figure 16



Smoking habits. No significant difference has been demonstrated between the mean values for Ind. M.B.C. in the smoking groups.

O.S.	(7)	=	95 L/min
S1	(12)	=	71 L/min
S2/3	(28)	=	100 L/min
E.S.	(5)	=	85 L/min

The unexpectedly high value for smokers in group S2/3 is probably explained by the fact that the younger men were all in this group.

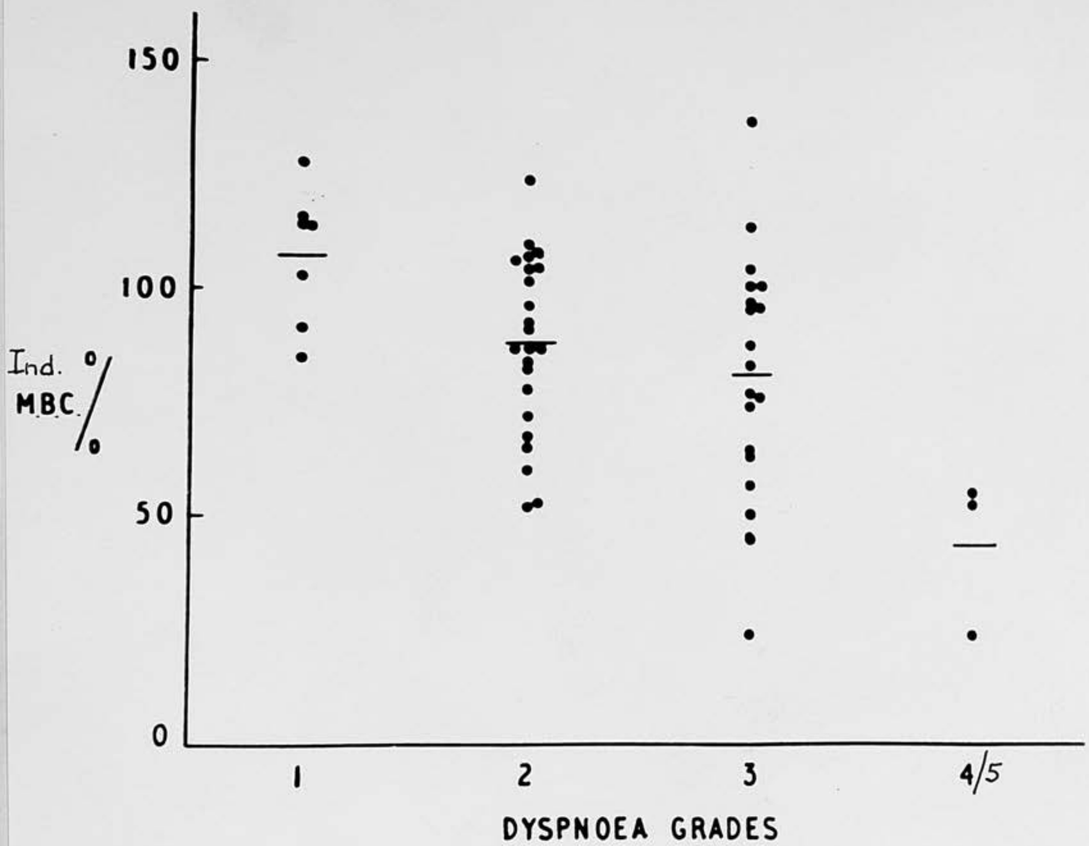
Dyspnoea. A highly significant relationship exists between Ind. M.B.C. and the dyspnoea grade ($F = 6.4$, $P < 0.01$).

Dyspnoea grade	1	(7)	=	120 L/min
" "	2	(23)	=	95 L/min
" "	3	(19)	=	82 L/min
" "	4/5	(3)	=	46 L/min

This relation persists when Ind. M.B.C. is expressed as a percentage of the normal value which takes age into account.

Figure 17 shows the relationship between Ind. M.B.C.% and the dyspnoea grade.

Figure 17



(ii) <u>The ratio of the maximum expiratory flow rate to the maximum inspiratory flow rate</u> $\left(\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}\right)$

It is considered that M.E.F.R. alone gives no more information about ventilatory function than Ind. M.B.C. However, when it is compared with M.I.F.R. more information may be obtained about the underlying nature of the ventilatory defect (McNeill, Malcolm and Brown, 1959). Normally the M.E.F.R. is greater than the M.I.F.R. and consequently the ratio is greater than 1. In emphysema the basic mechanical defect results in an inward collapse of the bronchial walls during expiration which results in a greatly reduced M.E.F.R. However, unless there are other important causes of increased airway resistance, such as bronchial secretions or smooth muscle spasm, inspiration is little affected. The result is that the normal $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ ratio is reduced and values well below 1 are obtained. The reason for examining this ratio, therefore, is to see if the pattern which is characteristic of "pure" emphysema emerges in any of the groups.

The measurements were made in all subjects and the best of 3 was accepted for both M.E.F.R. and M.I.F.R. The mean value for $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ for the whole group is 1.25 and the standard deviation is 0.59.

Age. There are no significant differences between mean $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ ratios in the age groups, although they do fall as age increases ($F < 1$).

49 and under (8)	=	1.51
50 to 59 (25)	=	1.23
60 and over (19)	=	1.08

X-ray category. There are no significant differences between mean $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ ratios in the X-ray categories.

Category	1	(17)	=	1.24
"	2	(13)	=	1.43
"	3	(4)	=	1.44
"	A	(11)	=	1.12
"	B+	(7)	=	1.04

Chronic bronchitis. There is no significant difference between the mean $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ ratios for those with and without chronic bronchitis.

Without chronic bronchitis (28)	=	1.30
With chronic bronchitis (24)	=	1.15

Smoking habits. There are no significant differences between the mean $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ ratios in the smoking groups.

O.S. (7) = 1.20

S1 (12) = 1.15

S2/3 (28) = 1.36

E.S. (5) = 0.96

Dyspnoea. Although the mean values for $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ fall consistently with increasing dyspnoea, the differences do not reach significant levels because of the scatter within the grades.

Dyspnoea grade 1 (7) = 1.64

" " 2 (23) = 1.26

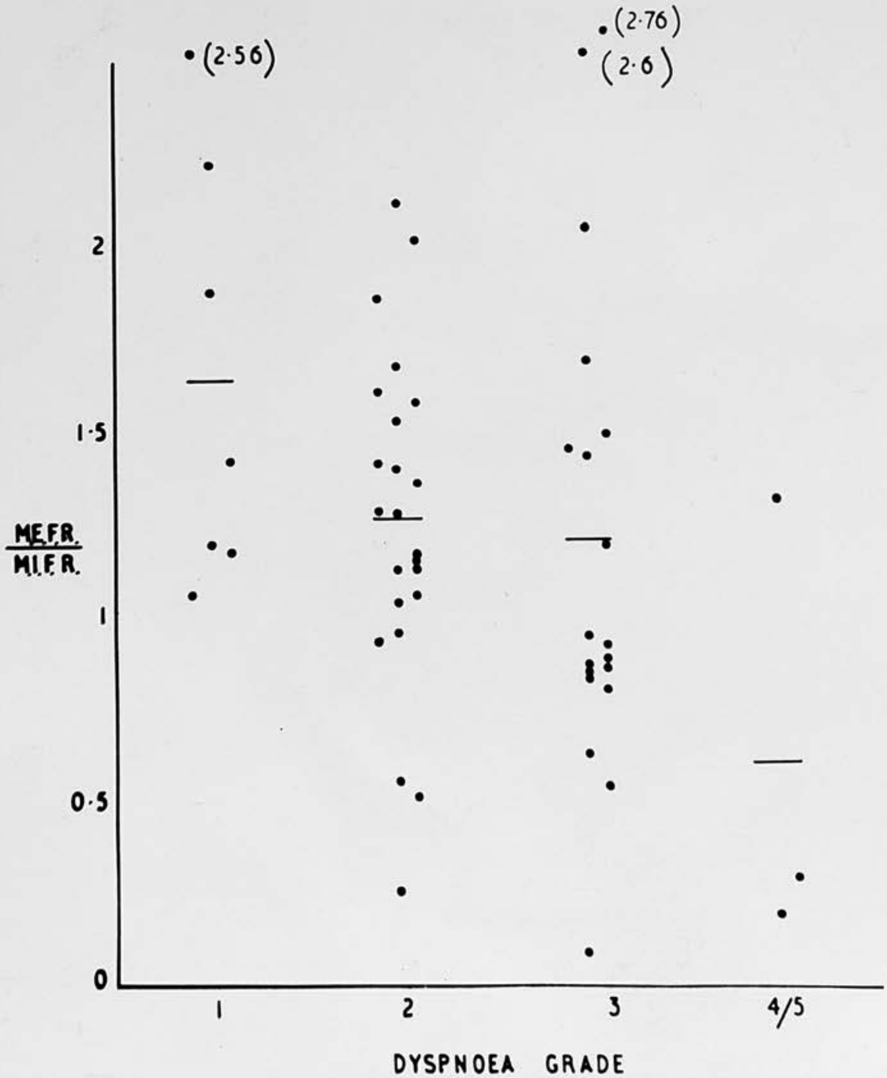
" " 3 (19) = 1.20

" " 4/5 (3) = 0.60

The ratio is only clearly below unity in dyspnoea grade 4/5 where the numbers are small.

Figure 18 shows the relationship of $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ to dyspnoea.

Figure 18



3. Lung Volumes

(i) Vital capacity (V.C.)

This was measured in all subjects and in each the best of 3 measurements was accepted. The mean V.C. for the whole group is 4004 ml and the standard deviation is 871 ml.

Expressed as a percentage of normal the mean V.C. is 107.8% and the standard deviation 22.5%.

Age. There are highly significant differences between the mean V.C. values in the age groups ($F = 8.6$, $P < 0.001$).

49 and under (7) = 5036 ml

50 to 59 (25) = 3800 ml

60 and over (19) = 3839 ml

The obvious difference is between the youngest age group and the others and not between the two older age groups. When V.C. is expressed as a percentage of the predicted value which takes age into account, the differences are less obvious but still significant ($F = 3.6$, $P < 0.05$).

<u>X-ray category</u>. There are no significant differences between mean V.C. values in the X-ray categories.

Category	1	(17)	=	4275 ml
"	2	(13)	=	3695 ml
"	3	(4)	=	3624 ml
"	A	(11)	=	4167 ml
"	B+	(7)	=	3879 ml

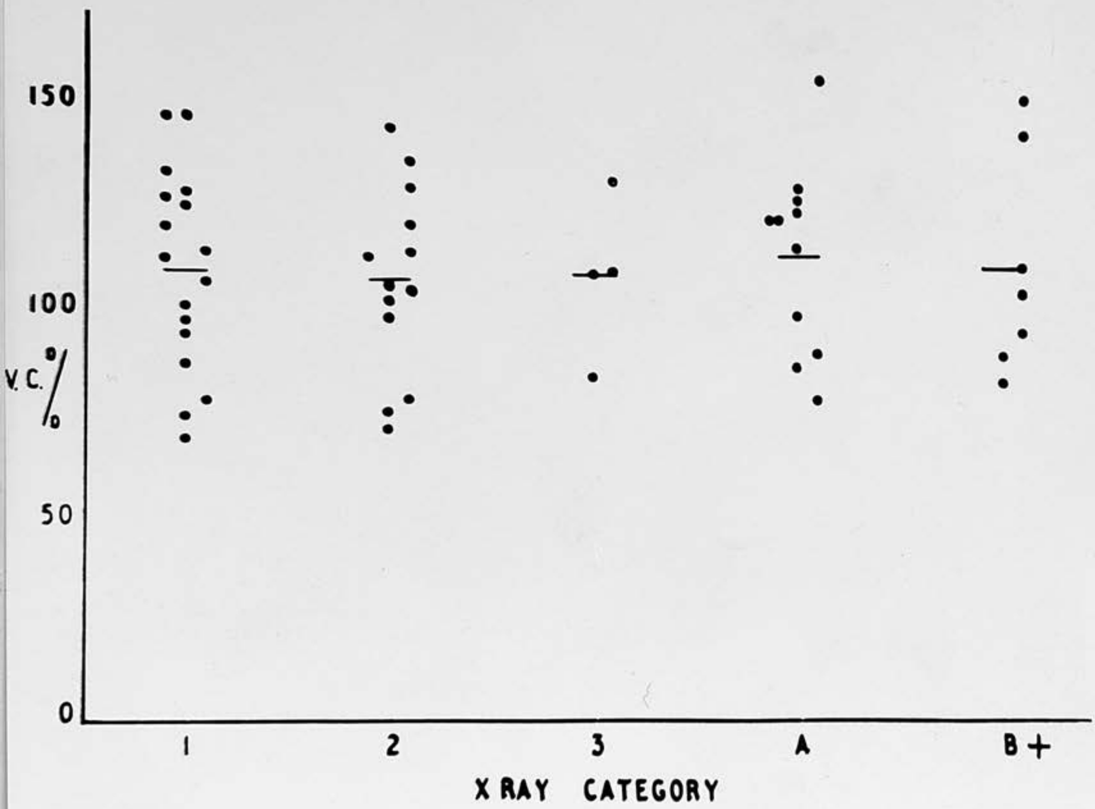
When V.C. is expressed as a percentage of normal the differences are still not significant.

Figure 19 illustrates the lack of relationship between V.C.% and X-ray category.

<u>Chronic bronchitis</u>. There is no significant difference between the mean V.C. for those with and without chronic bronchitis.

Without chronic bronchitis (28)	=	4143 ml
With chronic bronchitis (24)	=	3842 ml

Figure 19



Smoking habits. The differences in mean V.C. values between the smoking groups are just significant ($F = 2.91$, $P < 0.05$).

O.S.	(7)	=	3762 ml
S1	(12)	=	3462 ml
S2/3	(28)	=	4251 ml
E.S.	(5)	=	4263 ml

There is no apparent trend between the groups and the differences are not altered by expressing V.C. as a percentage of normal.

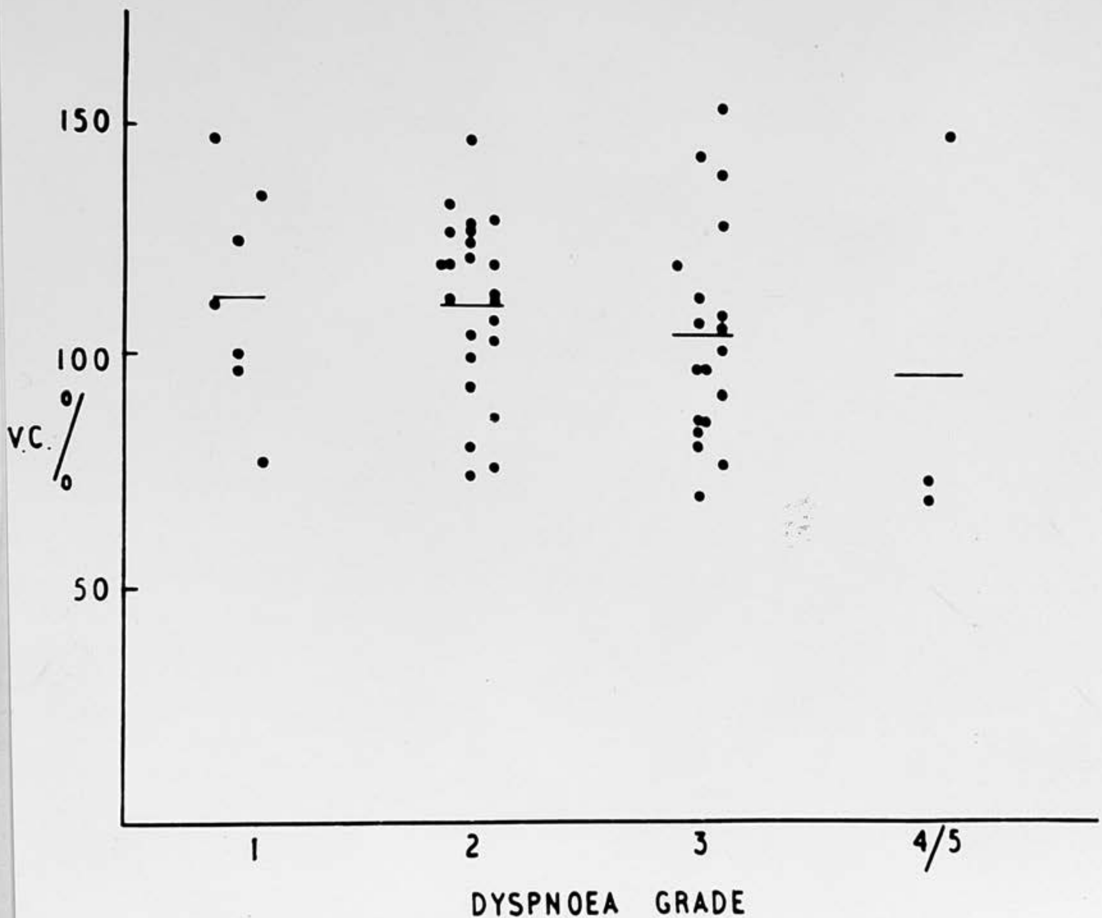
Dyspnoea. There are no significant differences between mean V.C. values in the dyspnoea grade ($F = 2.04$, $0.2 > P > 0.05$).

Dyspnoea grade	1	(7)	=	4576 ml
" "	2	(23)	=	4086 ml
" "	3	(19)	=	3787 ml
" "	4/5	(3)	=	3414 ml

When expressed as a percentage of normal the differences are still not significant.

Figure 20 shows the lack of relationship between V.C.% and the dyspnoea grades.

<u>**Figure 20**</u>



(ii) Total lung capacity (T.L.C.)

This was calculated in all subjects and the mean value is 7019 ml with a standard deviation of 1224 ml. Expressed as a percentage of the normal predicted value the mean T.L.C. is 112% and the standard deviation is 17.2%.

Age. There are significant differences between the mean values for T.L.C. in the age groups ($F = 3.5$, $P < 0.05$).

49 and under (8) = 7997 ml

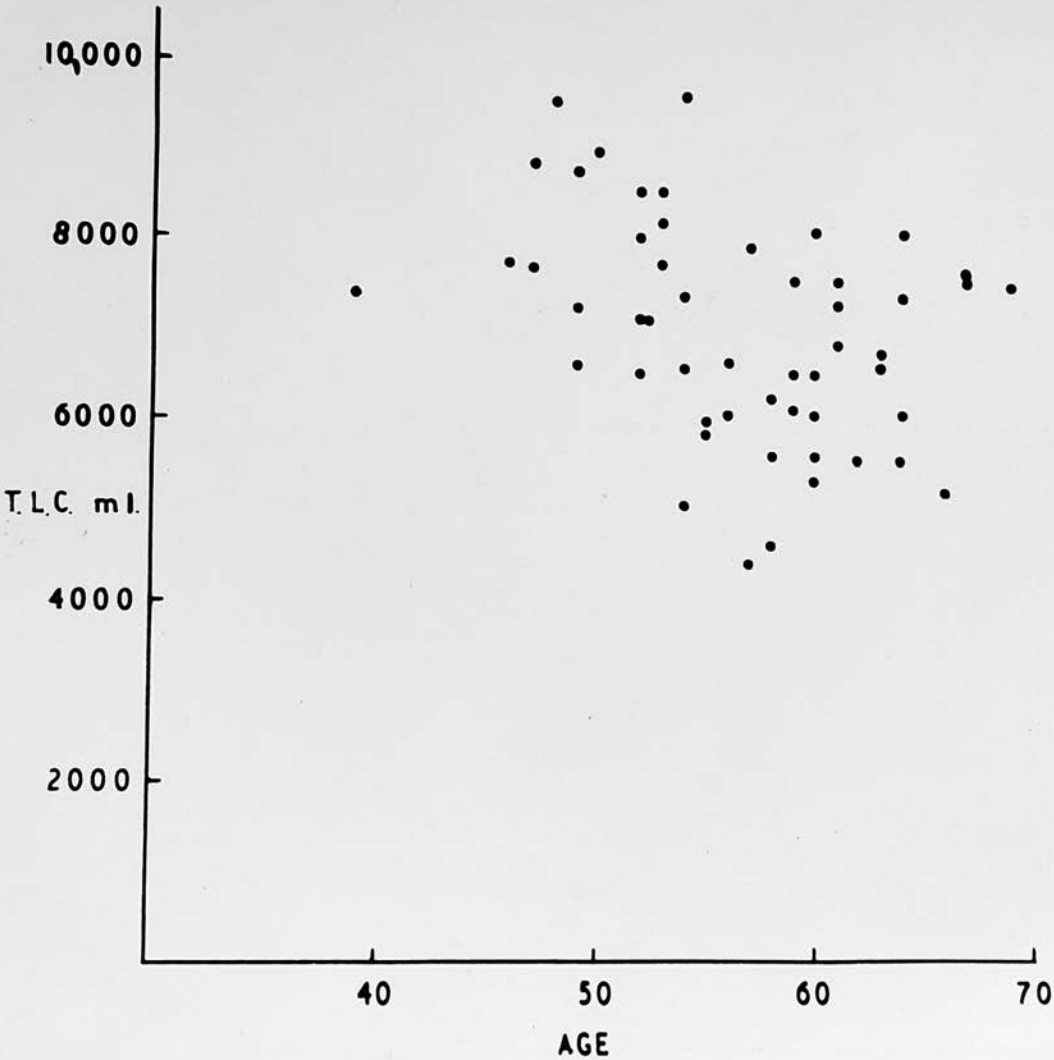
50 to 59 (25) = 6936 ml

60 and over (19) = 6716 ml

If T.L.C. is expressed as a percentage of normal this relationship is no longer apparent since age is taken into account in the prediction.

Figure 21 shows the relation between T.L.C. and age.

Figure 21



<u>X-ray category</u>. There are significant differences between the mean values for T.L.C. in the X-ray categories ($F = 4.1$, $P < 0.01$).

Category	1	(17)	=	7763 ml
"	2	(13)	=	6471 ml
"	3	(4)	=	6097 ml
"	A	(11)	=	7233 ml
"	B+	(7)	=	6420 ml

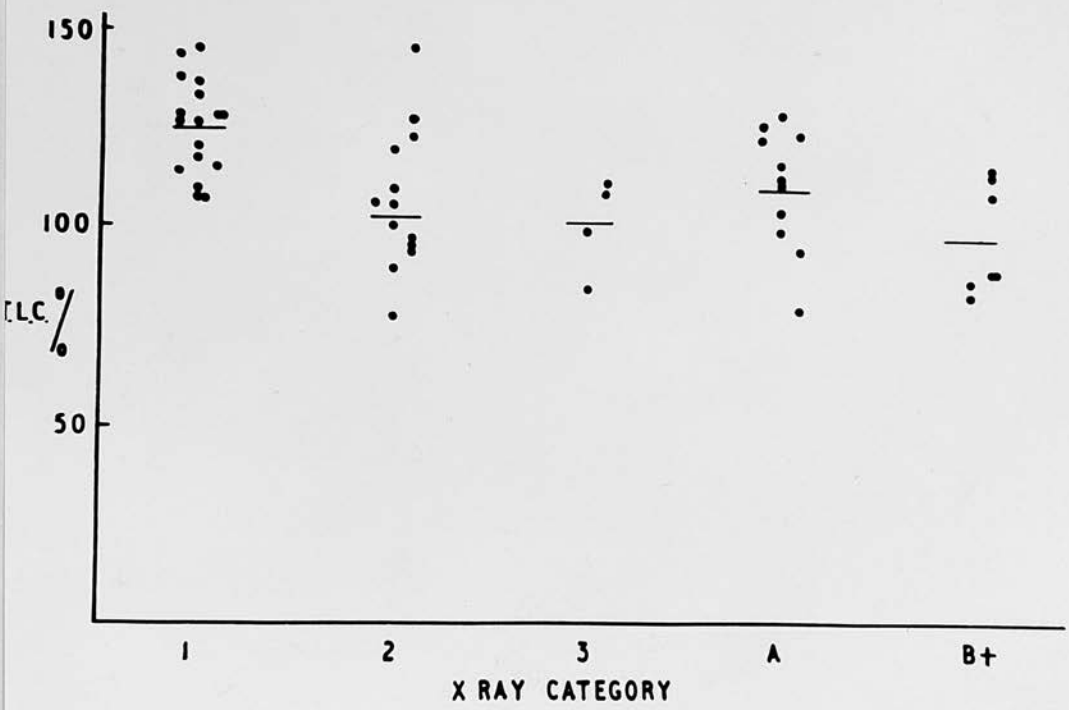
The trend with increasing radiological disease is irregular. The differences remain significant when T.L.C. is expressed as a percentage of normal ($F = 5.0$, $P < 0.01$).

Figure 22 shows the relationship between T.L.C.% and the X-ray categories.

<u>Chronic bronchitis</u>. There is no significant difference between the mean T.L.C. values for those with and without chronic bronchitis.

Without chronic bronchitis (28)	= 7013 ml
With chronic bronchitis (24)	= 7026 ml

Figure 22



<u>Smoking habits</u>. There are significant differences between the mean T.L.C. values in the smoking groups ($F = 2.55$, $P < 0.05$).

O.S.	(7)	=	6275 ml
S1	(12)	=	6529 ml
S2/3	(28)	=	7337 ml
E.S.	(5)	=	7451 ml

There is an apparent trend towards higher values as smoking increases which might have been attributed to age since the younger subjects were in group S2/3, but the differences remain significant even when age is allowed for by expressing T.L.C. as a percentage of normal ($F = 5.0$, $P < 0.01$).

<u>Dyspnoea</u>. There are no significant differences between the mean T.L.C. values in the dyspnoea grades.

Dyspnoea	grade	1 (7)	= 7212 ml
"	"	2 (23)	= 7113 ml
"	"	3 (19)	= 6829 ml
"	"	4/5 (3)	= 7049 ml

(iii) Residual volume expressed as a percentage of total lung capacity $\left(\frac{R.V.}{T.L.C.}\%\right)$

This was calculated in all subjects and the mean value is 42.8% with a standard deviation of 8.9%.

Age. There are no significant differences between the mean values for $\frac{R.V.}{T.L.C.}\%$ in the age groups.

49 and under (8)	=	39.4%
50 to 59 (25)	=	44.6%
60 and over (19)	=	42.9%

X-ray category. There are significant differences between the mean values for $\frac{R.V.}{T.L.C.}\%$ in the X-ray categories ($F = 2.8$, $P < 0.05$).

Category	1	(17)	=	45.2%
"	2	(13)	=	42.4%
"	3	(4)	=	40.8%
"	A	(11)	=	42.1%
"	B+	(7)	=	39.7%

The trend is irregular but the tendency is for this ratio to become smaller with radiological progression of the disease.

<u>Chronic bronchitis</u>. There is no significant difference between the mean values for $\frac{R.V.}{T.L.C.}\%$ in those with and without chronic bronchitis.

Without chronic bronchitis (28) = 40.9%

With chronic bronchitis (24) = 45.0%

<u>Smoking habits</u>. There are no significant differences between the mean values for $\frac{R.V.}{T.L.C.}\%$ in the smoking groups.

O.S. (7) = 39.4%

S1 (12) = 46.6%

S2/3 (28) = 42.0%

E.S. (3) = 42.8%

<u>Dyspnoea</u>. The differences between the mean values for $\frac{R.V.}{T.L.C.}\%$ in the dyspnoea grades are suggestive but not quite significant ($F = 2.44$, $0.2 > P > 0.05$).

Dyspnoea grade 1 (7) = 36.4%

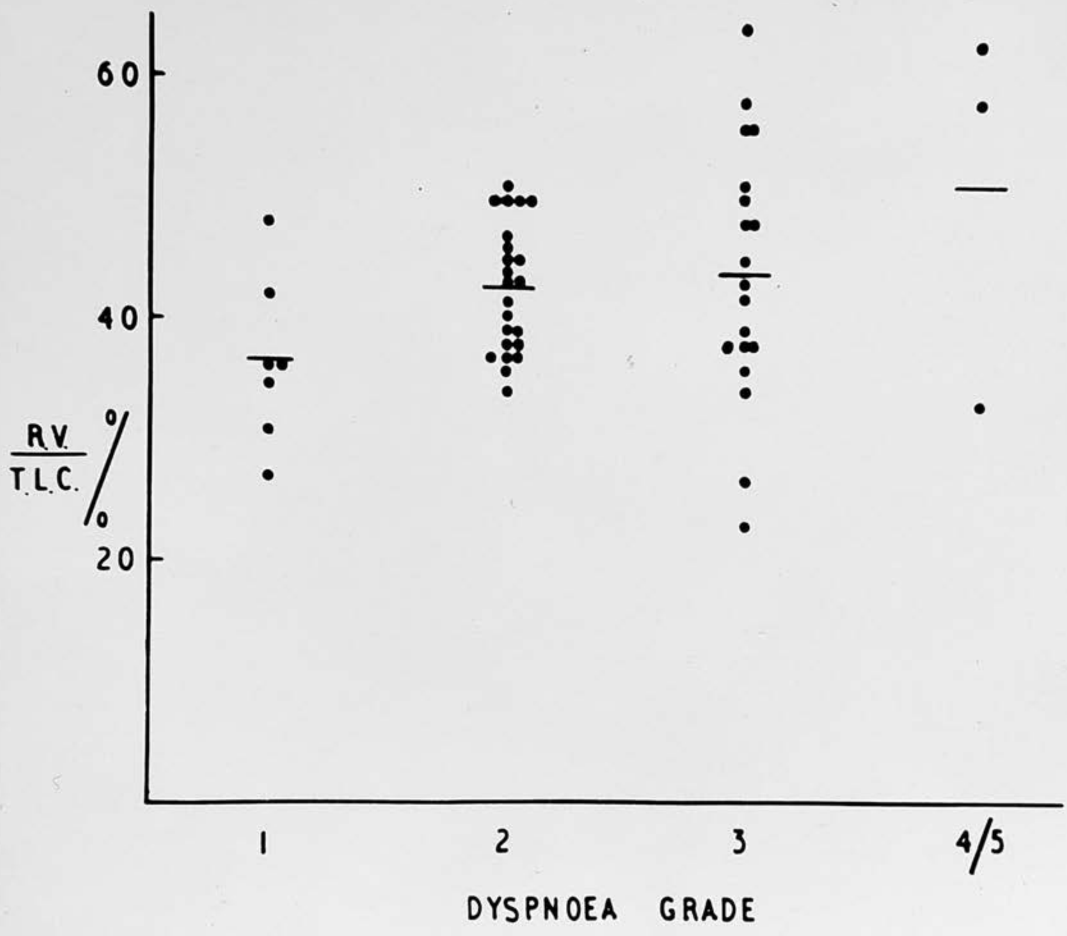
" " 2 (23) = 42.6%

" " 3 (19) = 43.9%

" " 4/5 (3) = 51.3%

Figure 23 shows the relationship between $\frac{R.V.}{T.L.C.}\%$ and the dyspnoea grades.

Figure 23



4. Lung Compliance

This was measured in 34 of the 52 miners by the method already described. A mean of the measurements over 3 respiratory cycles was taken. The mean compliance for the 34 miners is 253 ml/cm H_2O and the standard deviation is 91.4. The standard deviation of the 3 measurements on the same individual is 21.7 and the coefficient of variation is 8.6%.

Age. There are no significant differences between the mean compliance values of the age groups.

49 and under	(5)	= 280 ml/cm H_2O
50 to 59	(19)	= 242 ml/cm H_2O
60 and over	(10)	= 259 ml/cm H_2O

X-ray category. There are no significant differences between the mean compliance values of the X-ray categories.

Category	1	(14)	= 262 ml/cm H_2O
"	2	(6)	= 216 ml/cm H_2O
"	3	(1)	= 135 ml/cm H_2O
"	A	(8)	= 293 ml/cm H_2O
"	B+	(5)	= 229 ml/cm H_2O

Chronic bronchitis. There is no significant difference between the mean compliance values for those with and without chronic bronchitis.

Without chronic bronchitis (15) = 255 ml/cm H_2O

With chronic bronchitis (19) = 251 ml/cm H_2O

Smoking habits. There are no significant differences between the mean compliance of the smoking groups.

O.S. (5) = 168 ml/cm H_2O

S1 (8) = 266 ml/cm H_2O

S2/3 (17) = 268 ml/cm H_2O

E.S. (4) = 267 ml/cm H_2O

Dyspnoea. There are no significant differences between the mean compliance values of the dyspnoea grades.

Dyspnoea grade 1 (4) = 220 ml/cm H_2O

" " 2 (16) = 270 ml/cm H_2O

" " 3 (11) = 230 ml/cm H_2O

" " 4/5 (3) = 255 ml/cm H_2O

5. Blood Findings

(i) Haemoglobin (Hb G%)

This was measured in all subjects and the mean value is Hb = 15.3 G% with a standard deviation of 1.2 G%.

Age. There are significant differences between mean Hb values in the age groups ($F = 3.2$, $P < 0.05$).

49 and under (8)	=	16.2 G%
50 to 59 (25)	=	15.0 G%
60 and over (19)	=	15.2 G%

The trend between the groups is not regular but the younger men have higher values.

Figure 24 shows the relationship between Hb and age.

X-ray category. There are significant differences between the mean Hb values in the X-ray categories ($F = 4.2$, $P < 0.01$).

Category	1	(17)	=	16.0 G%
"	2	(13)	=	15.2 G%
"	3	(4)	=	13.9 G%
"	A	(11)	=	14.8 G%
"	B+	(7)	=	15.0 G%

The trend between groups is irregular and the highest mean value is in category 1. This may be because most of the young miners were in this group.

Figure 25 shows the relationship between Hb and X-ray category. ~~with the age groups indicated.~~

Figure 24

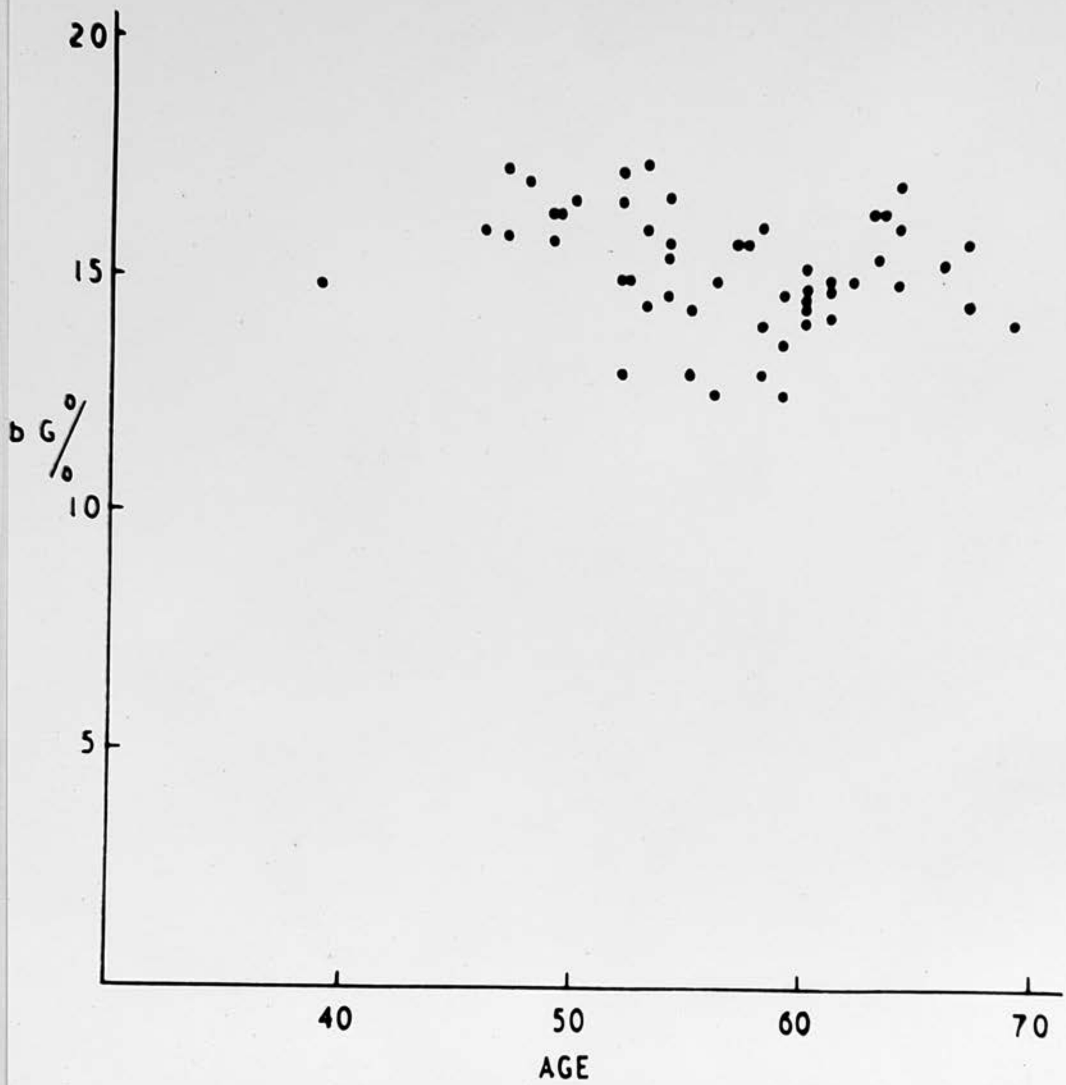
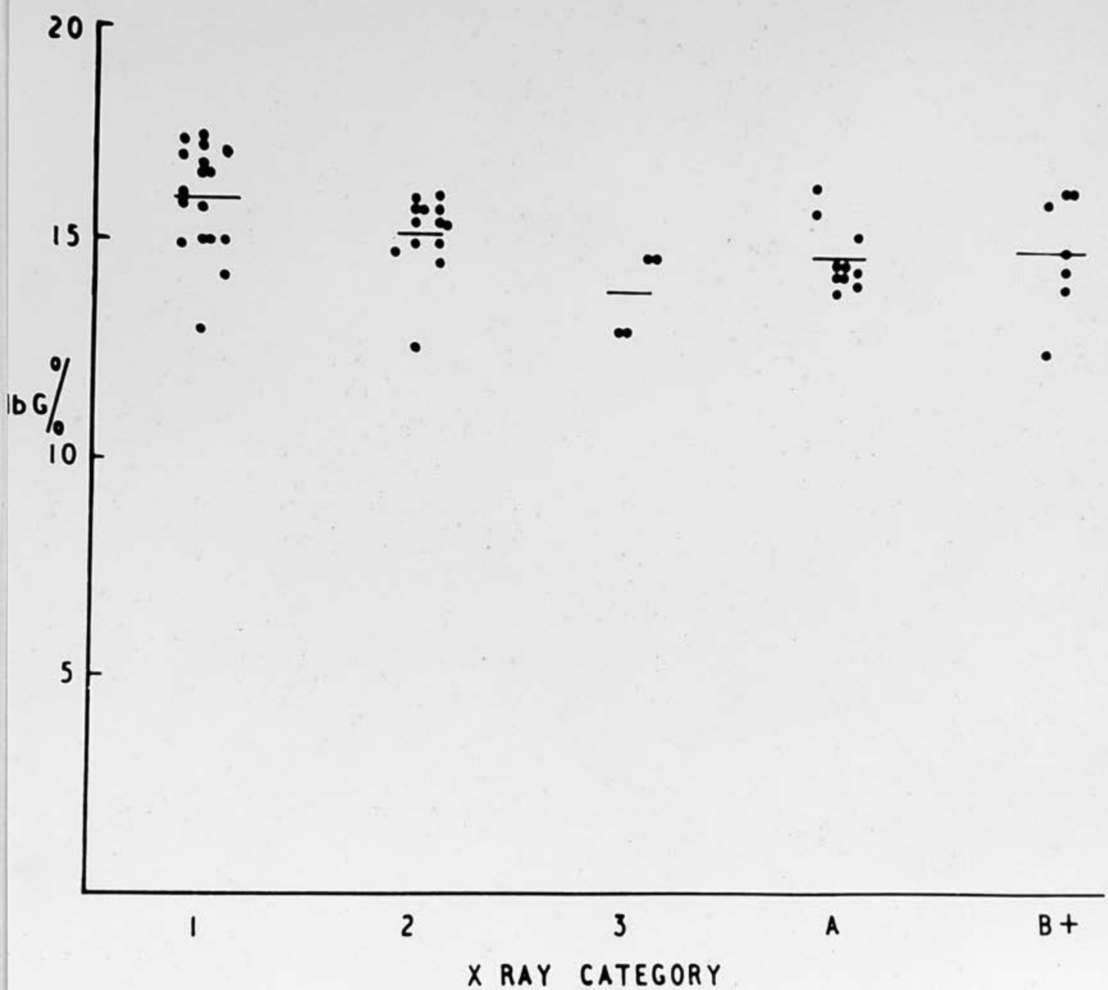


Figure 25



Chronic bronchitis. There is no significant difference between the mean Hb values for those with and without chronic bronchitis.

Without chronic bronchitis (28) = 15.5 G%

With chronic bronchitis (24) = 15.0 G%

Smoking habits. There are no significant differences between the mean Hb values in the smoking groups.

O.S. (7) = 15.4 G%

S1 (12) = 14.9 G%

S2/3 (28) = 15.9 G%

E.S. (5) = 15.8 G%

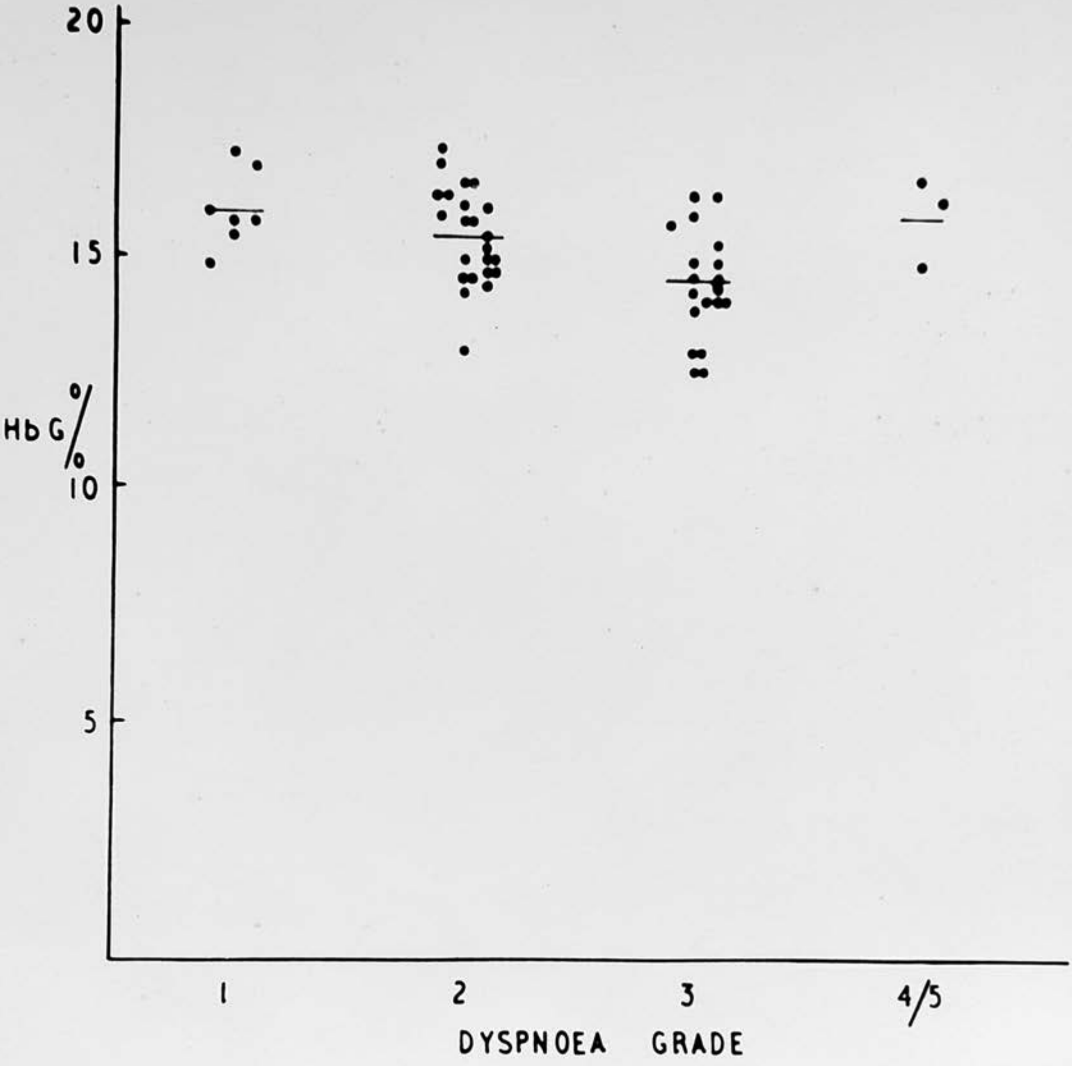
Dyspnoea. There are significant differences between the mean Hb values in the dyspnoea grades ($F = 4.5$, $P < 0.01$).

Dyspnoea grade	1	(7)	= 16.0 G%
" "	2	(23)	= 15.5 G%
" "	3	(19)	= 14.6 G%
" "	4/5	(3)	= 16.0 G%

The rise in mean value for dyspnoea grade 4/5 upsets the general trend but it may have a physiological explanation as a similar directional change is seen when the CO_2 content of venous blood is considered.

Figure 26 shows the relationship between Hb and dyspnoea. ~~and indicates the age groups~~.

Figure 26



(ii) <u>CO_2 content of venous blood (CO_2 mM/L)</u>

This was measured in 48 of the 52 miners. The mean value is 31.9 mM/L and the standard deviation 2.8 mM/L. For correlation between the tests, average values have been supplied for the 4 in whom the measurement was not made.

<u>Age</u>. There are no significant differences between mean values for CO_2 content in the age groups.

49 and under (8)	= 30.9 mM/L
50 to 59 (25)	= 32.6 mM/L
60 and over (19)	= 31.4 mM/L

<u>X-ray category</u>. There are no significant differences between the mean values for CO_2 content in the X-ray categories.

Category	1	(17)	= 32.0 mM/L
"	2	(13)	= 31.8 mM/L
"	3	(4)	= 31.8 mM/L
"	A	(11)	= 31.0 mM/L
"	B+	(7)	= 33.0 mM/L

<u>Chronic bronchitis</u>. There is no significant difference in the value for CO_2 content of those with and without chronic bronchitis.

Without chronic bronchitis (28)	= 31.8 mM/L
With chronic bronchitis (24)	= 31.9 mM/L

Smoking habits. There are significant differences between the mean values for CO_2 content in the smoking groups ($F = 3.8$, $P < 0.05$).

O.S.	(7)	= 32.6 mM/L
S1	(12)	= 33.7 mM/L
S2/3	(28)	= 31.2 mM/L
E.S.	(5)	= 30.4 mM/L

There is no apparent trend between the mean values.

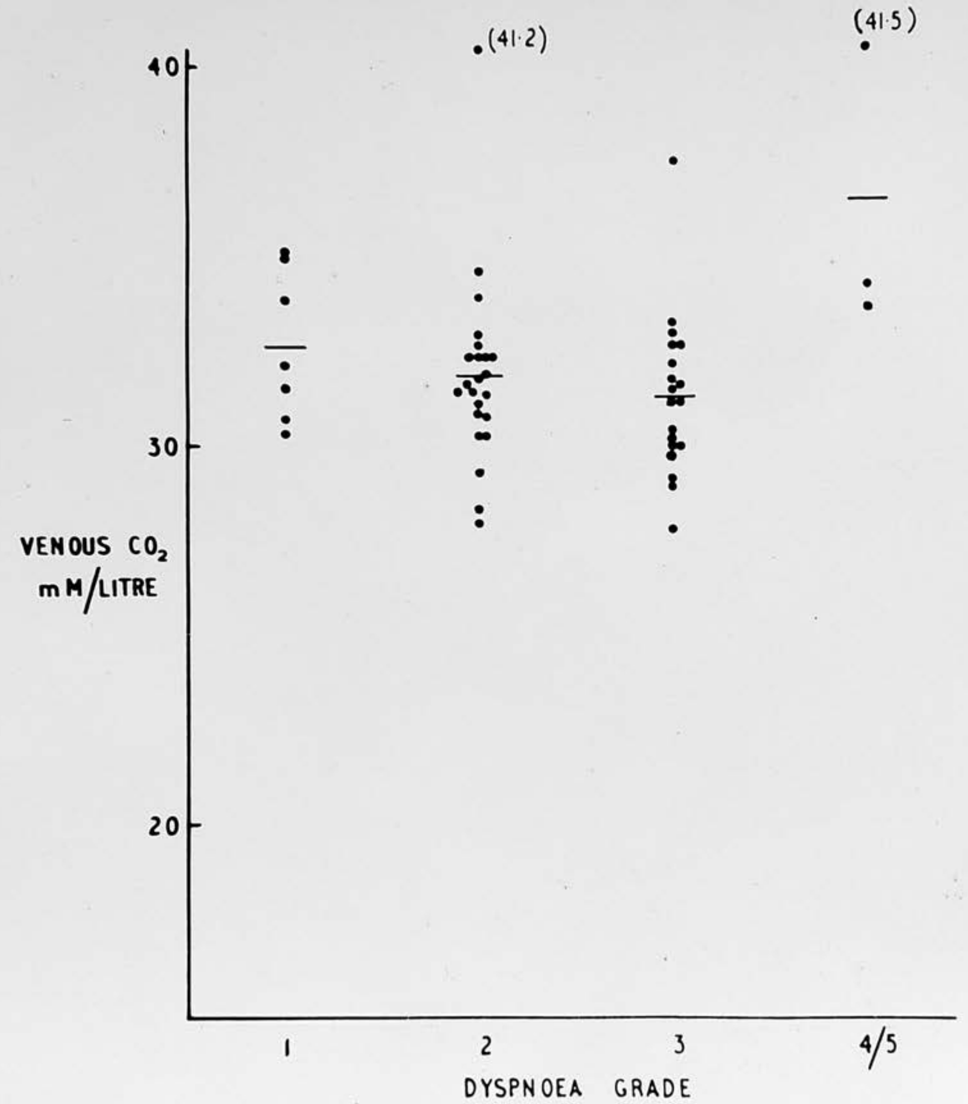
Dyspnoea. There are significant differences between the mean values for CO_2 content in the dyspnoea grades.

Dyspnoea	grade	1	(7)	= 32.5 mM/L
"	"	2	(23)	= 31.7 mM/L
"	"	3	(19)	= 31.1 mM/L
"	"	4/5	(3)	= 36.3 mM/L

As with Hb, the mean value for dyspnoea grade 4/5 is unexpectedly high. There is, in fact, a highly significant difference between this grade and the others ($F = 4.02$, $P < 0.01$). The probable explanation is that CO_2 retention was occurring only in the most disabled subjects.

Figure 27 shows the relationship between CO_2 content of venous blood and dyspnoea.

Figure 27



Summary of the relationship between physiological tests and the variables of age, X-ray category, chronic bronchitis, smoking habits and dyspnoea grades.

Each of the main variables has been divided into subgroups and the mean values in the subgroups have been compared in order to see if they are significantly different. If so, then the conclusion is that the subgroups for that particular variable are heterogeneous. It does not necessarily follow that a regular trend can then be demonstrated between the subgroups and, in fact, often this was not possible. This applies particularly to X-ray category A in which the results were frequently higher than expected. This may be due to several causes, (1) that the miners in this category were unusually fit, or (2) that the miners in the preceding category were unusually handicapped, or (3) that category A itself is wrongly placed in the sequence of radiological deterioration. It may be that the background of simple pneumoconiosis, rather than the small indefinite area of confluence, is the factor which influences the results of the physiological tests. There is evidence to suggest that this is so in respect of DL_{CO}. Of the 11 miners in category A, 6 had a background of category 2 simple pneumoconiosis and 5 a background of category 3.

The effect of expressing the results as a percentage of the predicted normal value is variable. In respect of DL_{CO}, by removing the variability due to body size, an already suggestive relationship to dyspnoea is enhanced and significant differences within the smoking groups are revealed. It is however difficult to interpret the differences in the smoking groups because there is no regular trend.

In respect of Ind. M.B.C., V.C., and T.L.C. the use of the percentage value largely disposes of the effect of age but otherwise has little influence on the relationships.

Table XV relates each test to each variable and indicates where significant differences in the mean values of the subgroups have been found.

TABLE XV

Relationship between physiological tests and the variables of age, X-ray category, chronic bronchitis, smoking and dyspnoea.

Test	Age	X-ray	Bronchitis	Smoking	Dyspnoea
DL_{CO}	*	* *	-	-	-
DL_{CO}%	*	* *	-	*	*
Ind. M.B.C.	* *	-	-	-	* *
Ind. M.B.C.%	-	-	-	-	* *
$\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$	-	-	-	-	-
V.C.	***	-	-	*	-
V.C.%	*	-	-	*	-
T.L.C.	*	* *	-	*	-
T.L.C.%	-	* *	-	* *	-
$\frac{\text{R.V.}}{\text{T.L.C.}}$%	-	*	-	-	-
Hb	*	* *	-	-	* *
Venous CO_2	-	-	-	*	* *

Significant differences in the subgroups of each variable are indicated by *. The levels of significance are * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Interrelationship between tests

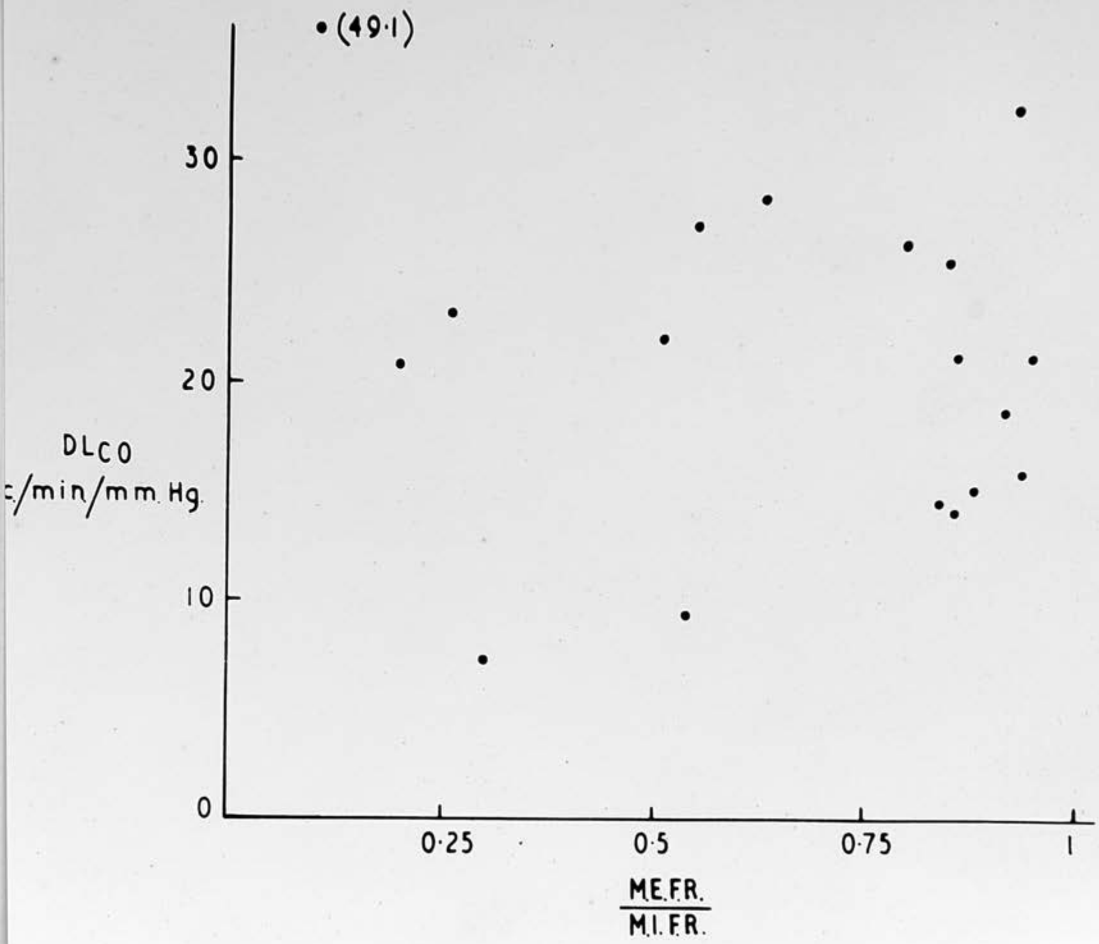
The specificity and independence of DL_{CO} from other tests of lung function is of particular importance if conclusions are to be drawn about the diffusing capacity of the lungs in pneumoconiosis.

Diffusing capacity and ventilatory function

(i) DL_{CO} and Ind. M.B.C. There is no significant relationship between these tests (correlation coefficient 0.017, standard error 0.141). Any condition which increases the expiratory resistance offered by the airways such as asthma, emphysema, or anatomical kinking of the airways, impairs the Ind. M.B.C. Other conditions affecting the chest wall and neuromuscular co-ordination also impair the Ind. M.B.C. The conclusion, therefore, is that none of these conditions which may or may not have been present, systematically influenced the results of DL_{CO}.

(ii) DL_{CO} and $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ ratio. It has been suggested already that a marked reduction in the ratio $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$ indicates the structural changes of emphysema. Since it has been shown that the diffusing capacity of the lungs may be severely impaired in emphysema (Bates, Knott and Christie, 1956; Ogilvie, 1959; Macnamara, Prime and Sinclair, 1959) it is important to see if a significant relationship exists between DL_{CO} and $\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$. Figure 28 shows that no such relationship exists.

Figure 28



Diffusing capacity and lung size

The influence of body size on DL_{CO} has been mentioned. The importance of alveolar volume in the equation for calculating DL_{CO} has also been referred to. A relationship, therefore, might be expected between DL_{CO} and T.L.C. because that volume is close to the alveolar volume of the subject during measurement of DL_{CO}.

There is in fact a significant relationship between DL_{CO} and T.L.C. (correlation coefficient 0.401, standard error 0.141, $P < 0.01$) and Figure 29 shows this relationship.

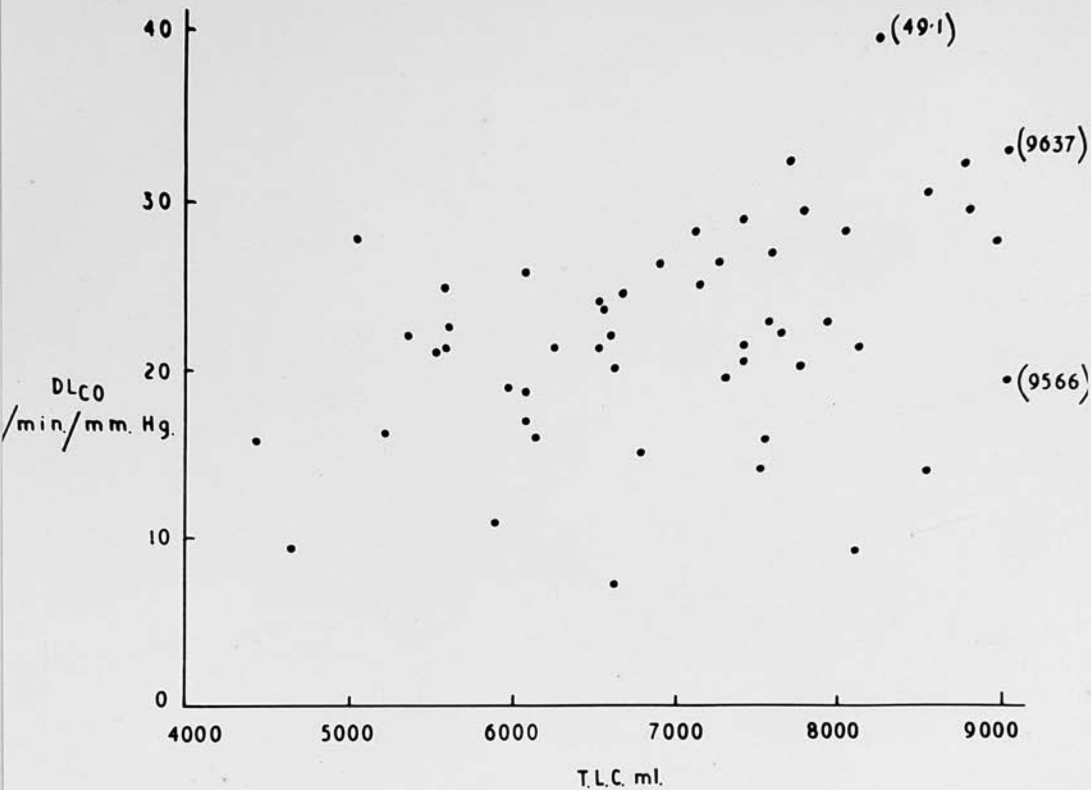
Diffusing capacity and lung compliance

If a reduction in diffusing capacity of the lungs results either from a reduction in the total area available for diffusion or from a fibrogenic reaction in the septal tissues, both DL_{CO} and compliance might be reduced together. The differences between the mean DL_{CO} values in 5 compliance subgroups are not quite significant ($F = 2.0$, $0.20 > P > 0.05$).

Compliance 150 ml/cm H_2O (4) = 18.2 ml/min/mmHg
Compliance 150/249 " " (15) = 25.9 " "
Compliance 250/349 " " (9) = 21.1 " "
Compliance 350 " " (6) = 26.6 " "

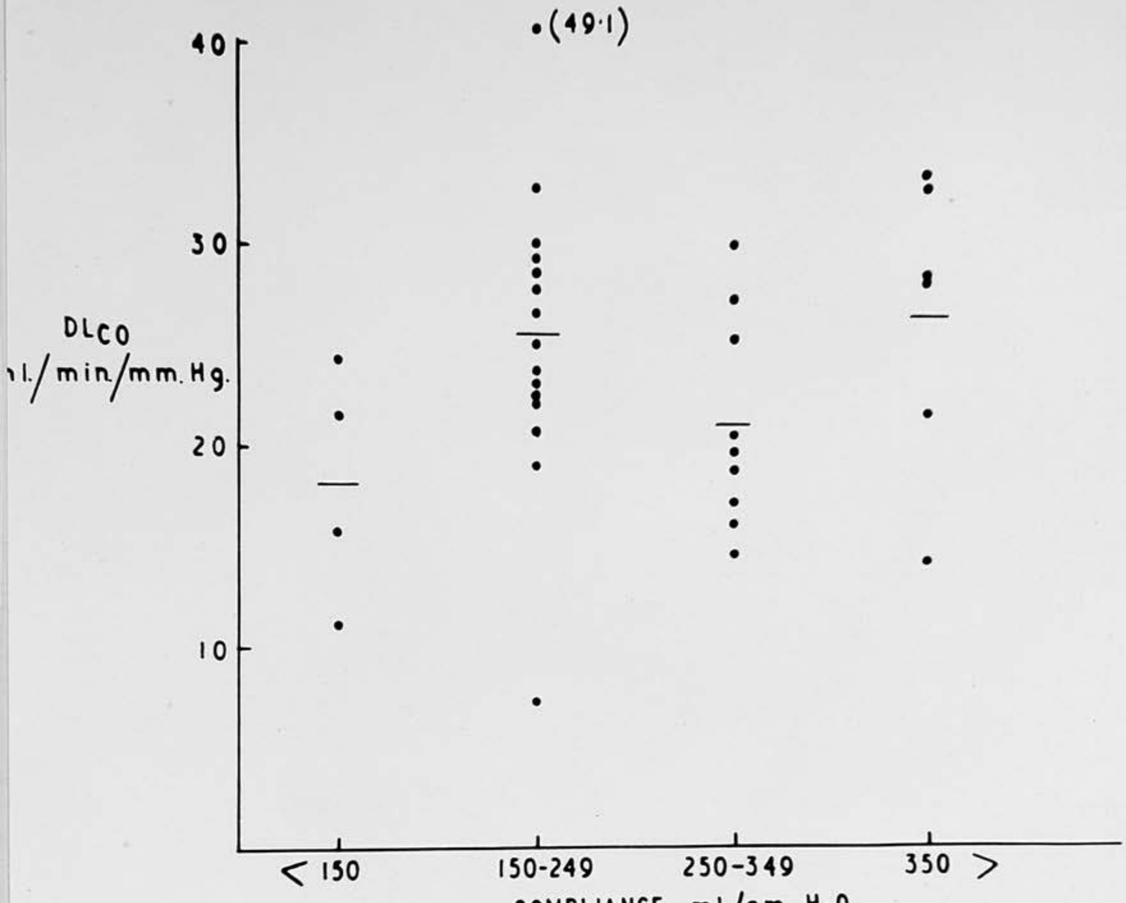
Figure 30 shows the relationship between compliance and DL_{CO}.

Figure 29



40
30
20
10
0
DLCO
/min./mm. Hg.
4000
5000
6000
7000
8000
9000
T.L.C. ml.
(49·1)
(9637)
(9566)

Figure 30


(49·1)
40
30
20
10
DLCO
ml./min./mm. Hg.
< 150
150-249
250-349
350 >
COMPLIANCE ml./cm. H2O.

Diffusing capacity and haemoglobin

In diffusing from alveolus to capillary blood to combine with haemoglobin, carbon monoxide meets two resistances. The first is the pulmonary membrane and the second is the rise in plasma tension of carbon monoxide resulting from the time taken for the chemical reaction $CO + Hb \rightarrow COHb$ to occur within the red cell. It has been calculated that about half the total resistance to diffusion is due to the delay caused by this reaction (Roughton and Forster, 1957; McNeill, Rankin and Forster, 1958). The reaction time is influenced by the amount of haemoglobin present and anything that reduces this, such as destruction of the capillaries by disease or anaemia, will also reduce DL_{CO}.

For this reason it is important to know if the subjects were anaemic or polycythaemic and if there is any relationship between Hb and DL_{CO}. The Hb values are given in Table III in the appendix where it can be seen that the lowest is 12.6 G% and the highest is 17.4 G%. The mean Hb value for the whole group is 15.3 G% and the standard deviation 1.2 G%.

No significant relationship has been found between DL_{CO} and Hb (correlation coefficient 0.033, standard error 0.141).

Table XVI summarises the relationships between diffusing capacity, ventilatory capacity, lung size and haemoglobin level.

TABLE XVI

Correlation coefficients of DL_{CO}, Ind. M.B.C., T.L.C., and Hb

	Ind. M.B.C.	T.L.C.	Hb
DL_{CO}	0.017	0.401**	0.033
Ind. M.B.C.		0.194	0.060
T.L.C.			0.302*

Standard error = 0.141.

*$P < 0.05$, **$P < 0.01$.

Partial coefficient between DL_{CO} and Hb (T.L.C. constant) = 0.101 which is not significant.

Lung compliance

The compliance of the lungs and chest wall of cats has been shown to be related to lung volume by Nisell and Dubois (1954). Marshall (1957) has analysed the physical properties of the lungs in man in relation to the subdivision of lung volume and has found that compliance correlates best with the functional residual capacity (F.R.C.).

In this study a significant relationship has also been found between compliance and F.R.C. ($F = 3.6$, $P < 0.05$). As the F.R.C. is reduced by about 700 ml, compliance is reduced by 100 ml/cm H_2O.

A significant relationship also exists between compliance and T.L.C. ($F = 3.2$, $P < 0.05$).

Figures 31 and 32 show the relationships between compliance and F.R.C., and compliance and T.L.C., respectively.

Figure 31

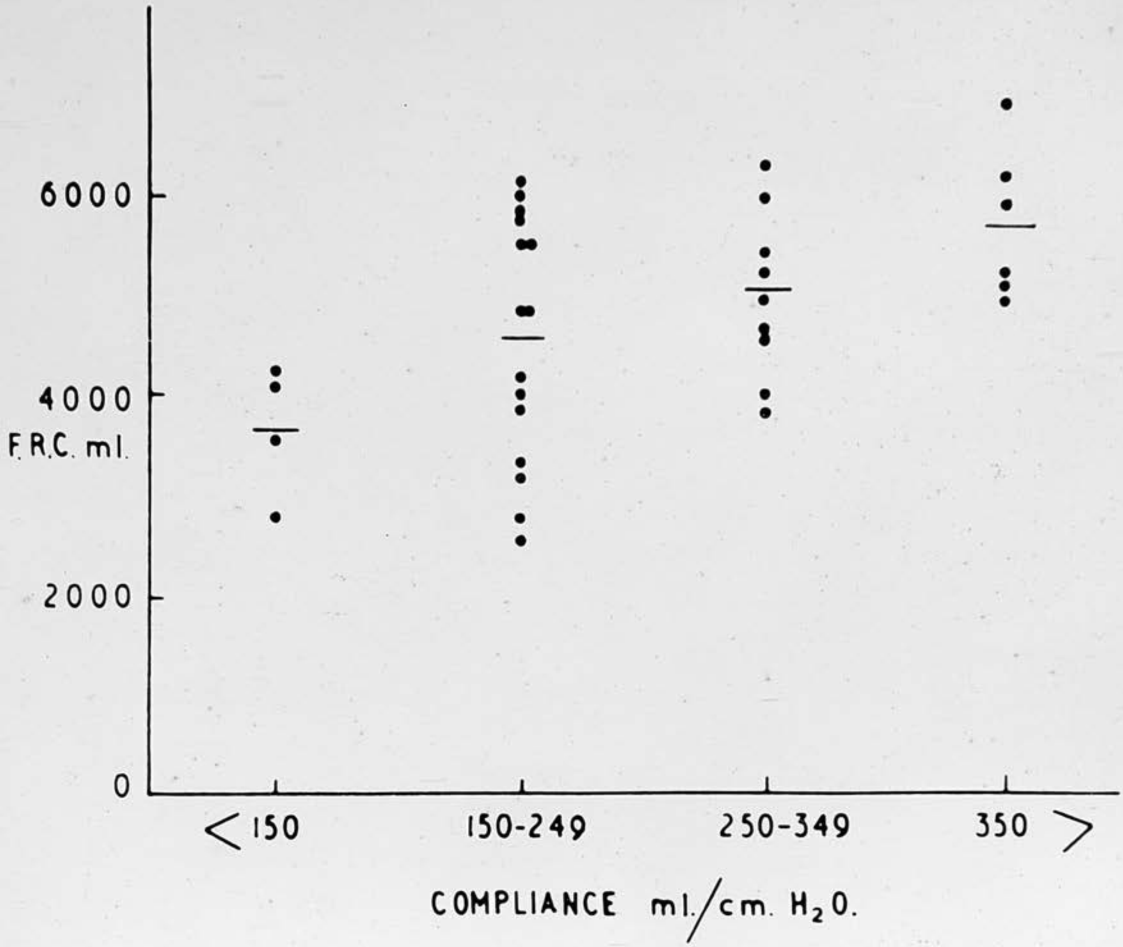
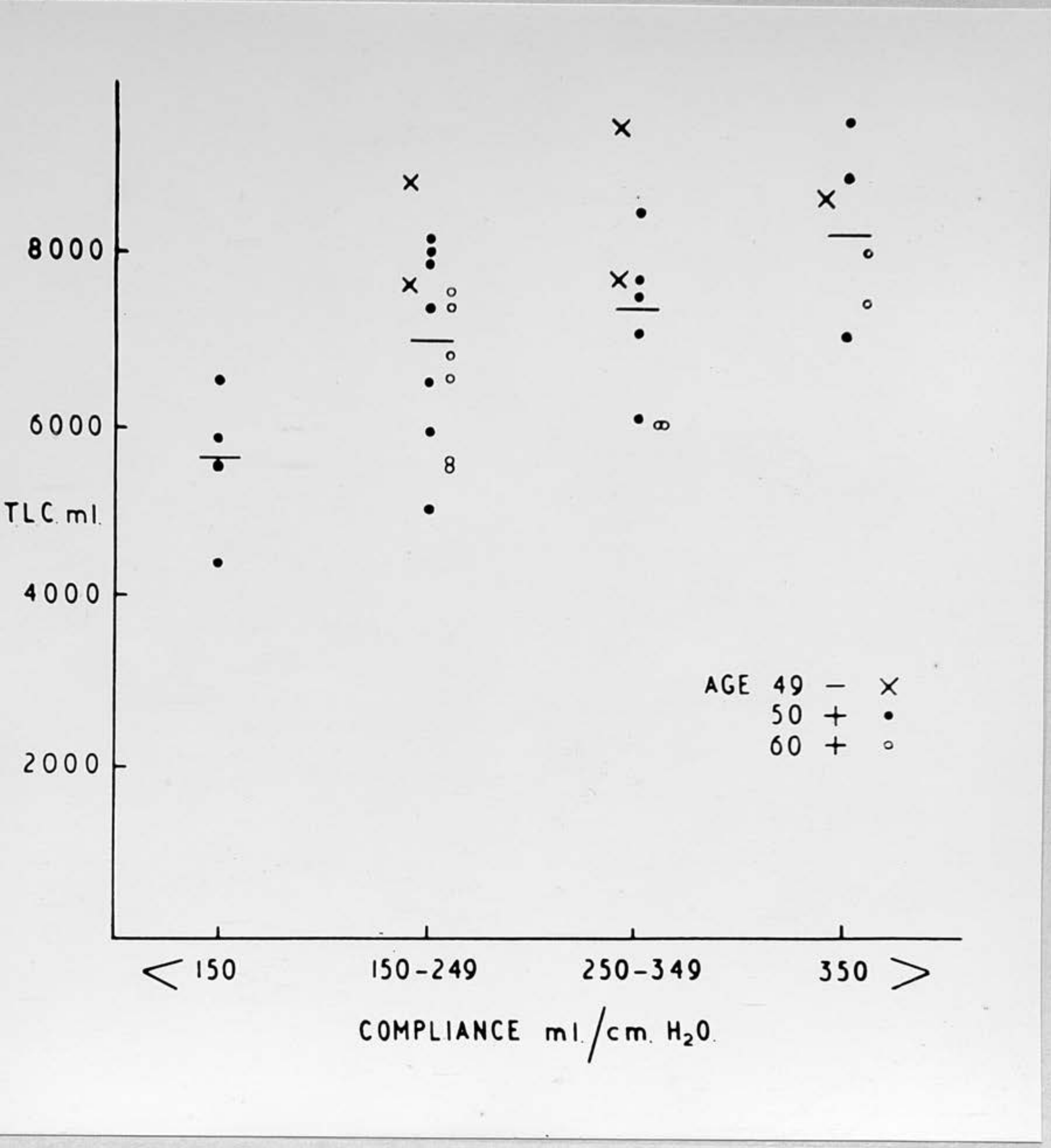

6000
4000
F.R.C. ml.
2000
0
<150
150-249
250-349
350 >
COMPLIANCE ml./cm. H_2O.

Figure 32


8000
6000
TLC ml.
4000
2000
AGE 49 – ×
50 + •
60 + ∘
< 150
150-249
250-349
350 >
COMPLIANCE ml/cm. H_2O

DISCUSSION

The method of selecting subjects for study is undoubtedly of great importance in the study of a disease such as pneumoconiosis. Gilson and Hugh-Jones (1955) frequently refer to the disadvantages of hospital selection where a bias towards the more disabled is to be expected, and Carpenter, Cochrane, Gilson and Higgins (1956) have illustrated the bizarre results that may be obtained in the measurement of the ventilatory capacity if a non-representative sample of the mining community is studied.

Because of these warnings, considerable efforts were made to include in this study miners who were free, or relatively free, from hospital bias. By studying miners from the Fitness Centre who were there on account of a non-respiratory disability, and by making special arrangements with the National Coal Board for miners to attend from home, it was possible to balance numerically those who were in hospital on account of pneumoconiosis at the time of study.

The final composition is not ideal but it transpires that there is no significant difference between the two main groups in respect of age, dyspnoea grade and ventilatory capacity. The reason for this is, almost certainly, that the miners from the Industrial Chest Diseases Unit at Bridge of Earn Hospital were there primarily for short term assessment and physiological studies and not for treatment of a respiratory disability.

Because of the defects in selection, reservations about the conclusions are necessary, but by relating each physiological test to age, clinical state and radiological category, genuine information should be obtained about the effects of coal dust in the lungs.

The general characteristics of the whole group will be discussed before the results of the physiological studies. Table VI is shown again for ease of reference.

<u>Age</u>. The miners are older than those studied by Gilson and Hugh-Jones (1955). Their subjects were in three age groups of 35, 45 and 55 years in each of which the range was restricted to ± 3 years. The miners in this study are virtually a decade older. The mean age is 56.6 years, the standard deviation 6.3 years and the groups used are 49 and under, 50 to 59 and 60 and over. With increasing age there is a known deterioration in pulmonary function. In addition, increasing age in miners means a longer period of exposure to dust, often with evidence of radiological progression, and therefore, the contribution

TABLE VI

	Age			X-ray category					Chronic bronchitis		Smoking habits				Dyspnoea grade			
	-49	50+	60+	1	2	3	A	B+	Absent	Present	OS	S1	S2/3	ES	1	2	3	4/5
Age																		
-49	8			5	1	-	2	-	7	1	-	-	8	-	2	5	1	-
50+		25		9	6	2	6	2	10	15	4	6	12	3	3	10	10	2
60+			19	3	6	2	3	5	11	8	3	6	8	2	2	8	8	1
X-ray																		
1	5	9	3	17					10	7	1	2	10	4	3	9	3	2
2	1	6	6		13				9	4	5	2	6	-	4	5	4	-
3	-	2	2			4			2	2	1	1	2	-	-	2	2	-
A	2	6	3				11		5	6	-	3	8	-	-	6	5	-
B+	-	2	5					7	2	5	-	4	2	1	-	1	5	1
Chronic bronchitis																		
-	7	10	11	10	9	2	5	2	28		6	3	16	3	6	13	8	1
+	1	15	8	7	4	2	6	5		24	1	9	12	2	1	10	11	2
Smoking																		
OS	-	4	3	1	5	1	-	-	6	1	7				2	3	2	-
S1	-	6	6	2	2	1	3	4	3	9		12			-	3	7	2
S2/3	8	12	8	10	6	2	8	2	16	12			28		5	15	7	1
ES	-	3	2	4	-	-	-	1	3	2				5	-	2	3	-
Dyspnoea																		
1	2	3	2	3	4	-	-	-	6	1	2	-	5	-	7			
2	5	10	8	9	5	2	6	1	13	10	3	3	15	2		23		
3	1	10	8	3	4	2	5	5	8	11	2	7	7	3			19	
4/5	-	2	1	2	-	-	-	1	1	2	-	2	1	-				3

The 3 age groups used are 49 and under, 50 to 59 and 60 and over.
X-ray categories as explained in text. Category B+ includes complicated pneumoconiosis of category B or more.
Under smoking habits, subgroups 2 and 3 are combined.
Under dyspnoea, grades 4 and 5 are combined.

of each factor to disability is difficult to determine.

In the Fife coalfields the incidence of pneumoconiosis is well below that in South Wales (see appendix) and the time taken to develop radiological evidence of the disease is longer. From a long experience of Pneumoconiosis Medical Panels in Scotland, Black (1953) reported that certified cases under the age of 41 were rare. The tempo of the disease is probably closer to that observed by McCallum and Newell (1958) in Northumberland where the prevalence levels were found to lag 5-13 years behind Durham and South Wales.

Information is slowly accumulating about the Scottish pits which are included in the Pneumoconiosis Field Research programme of the National Coal Board and I am indebted to Dr. J. Rogan for the information that the period of exposure leading to 20% prevalence of category 1 or more pneumoconiosis in a Fife colliery is about 33 years for workers at the coal face. This is more than double the time for some collieries in South Wales. Thus the age of the miners in this study very probably reflects the later development of pneumoconiosis in Fife.

Symptomatology

(i) Breathlessness. Although this is regarded as the principal symptom of pneumoconiosis, it is necessary to remember that it is also the main symptom of other respiratory diseases, such as emphysema, cardiac disease and anaemia. Thus of the three most breathless miners, one had advanced pneumoconiosis radiologically but two had only simple pneumoconiosis of category 1 and presumably had some cause other than that for their breathlessness. Nevertheless, the least breathless miners (dyspnoea grade 1) were all in the early X-ray categories and there was a general tendency for increasing breathlessness to be associated with increasing radiological abnormality. In the questions about breathlessness the subject was asked to relate his disability to a normal man of his own age and therefore, the effect of age alone should not be apparent. Although the miners in age group 49 and below were mainly in dyspnoea grades 1 and 2, those in the two older age groups 50 to 59 and 60 and over, were evenly distributed between dyspnoea grades 2 and 3.

The high correlation between dyspnoea and the ventilatory capacity (r = 0.77) obtained by Gilson and Hugh-Jones (1955), led Carpenter, Cochrane, Gilson and Higgins (1956) to substitute the Ind. M.B.C. for the subjective dyspnoea grades. A comparison between measurements of the ventilatory capacity in different studies should, therefore, give an indication of relative disabilities. The mean values for Ind. M.B.C. given by Carpenter et al. (1956) for the age group 55 to 64 years in three random samples were:-

Category 1 = 90.3 L/min
" 2 = 78.4 L/min
" 3 = 76.8 L/min

The mean values for the direct M.B.C. given by Gilson and Hugh-Jones (1955) for a group whose mean age was 55 years, were:-

Category 1 and 2 = 100 L/min
" 3 = 81 L/min

The mean values for the direct M.B.C. given by Lethart (1959) for a group of Durham miners whose mean age was 54 years, were:-

Category 1 = 78 L/min
" 2 = 89 L/min
" 3 = 77 L/min

In this study the mean age for all miners is 56.6 years (S.D. 6.3), and the corresponding values for Ind. M.B.C. are:-

Category 1 = 97 L/min
" 2 = 96 L/min
" 3 = 91 L/min

The conclusion, therefore, is that, judged by an objective test of disability, there is nothing to suggest that the miners in this study with simple pneumoconiosis are unduly handicapped.

(ii) Chronic bronchitis. Higgins, Oldham, Cochrane and Gilson (1956) investigated the incidence of chronic bronchitis in a random sample of the population of the industrial town of Leigh and used very similar questions to the ones employed in this study. The population of Leigh includes non-miners, miners and ex-miners and they found a significantly higher incidence of chronic bronchitis in the miners and ex-miners which could not be explained by differences in smoking habits or social class. The incidence was 26.7% in miners without pneumoconiosis and 12.9% in miners with pneumoconiosis. This is considerably lower than the incidence in this study which is 44%. Since the criteria for the diagnosis of chronic bronchitis were a little more severe than those of Higgins et al. (a productive cough was required to last most of the day and not just some part of it, and a history of a chest illness in the past three years was accepted only if it lasted more than one week), the higher incidence in this study is difficult to explain. Either it is genuine or a systematic bias has been operating which has resulted in the diagnosis of chronic bronchitis being made too often. When the results of the physiological tests are considered, the suspicion that the diagnosis has been made too readily persists because there is a recurring failure to show significant differences between those with and without chronic bronchitis. Generally the mean values for those with and those without chronic bronchitis do show differences in the expected direction, but significant levels are not attained. Table XVII shows the mean values for the two groups in respect of ventilatory function, lung volumes and diffusing capacity.

TABLE XVII

Test	Chronic bronchitis Absent	Chronic bronchitis Present
Ind. M.B.C. L/min	98.0	83.0
$\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}$	1.30	1.15
V.C. ml	4143	3842
$\frac{\text{R.V.}}{\text{T.L.C.}}$ %	40.9	45.0
DL_{CO} ml/min/mmHg	24.3	21.0

Recently, Fletcher, Elmes, Fairbairn and Wood (1959) have reviewed the methods of diagnosing chronic bronchitis and they indicate that, by sputum volume measurements and a gradation of the severity of bronchitis, a better correlation with the ventilatory capacity may be obtained. On reflection, it would have been better to introduce an objective measurement of the sputum volume in a study such as this.

The miners in the 49 and under age group were almost entirely free from bronchitis although they were all moderately heavy smokers. The frequency of bronchitis in the 50 to 59 and 60 and over age groups is similar.

Of the 24 miners who had chronic bronchitis, only one was a non-smoker. Two other bronchitics had smoked in the past but had since stopped. The converse, that smokers are likely to suffer from bronchitis, cannot be sustained because about half the smokers were unaffected. The younger miners, however, contribute largely to these and it may simply be a question of time before symptoms develop.

It is difficult to interpret the influence of smoking on the results of the pulmonary function studies. In some tests, a difference can be established between the smokers and non-smokers but it is often impossible to demonstrate a regular trend within the smoking groups.

This was the experience of Higgins (1959) who in the study of men in a similar age group, found a decrease in the ventilatory capacity with increasing smoking but only a significant difference between the non-smokers and smokers as a whole. The fact that the younger miners in this study are all in group S2/3 frequently boosts the results of this group and obscures any regular trend in the mean values. The ex-smokers are also a problem because it is not clear whether they should take an intermediate place between the non-smokers and smokers, or whether they should be placed at the end of the sequence, on the grounds that they stopped smoking because of increasing disability. Probably they should be discounted altogether, because they are a small group and contain the two subjects in whom the information about smoking was imprecise.

The analysis of smoking habits has contributed little towards the interpretation of the results of the pulmonary function studies. Nevertheless, smoking is a factor that demands attention in the study of any respiratory disease and had to be included.

(iii) Cardiac disease. There was no attempt to exclude, by previous examination, any miner with evidence of cardiac disease. As it happened, there was no evidence of cardiac failure in any of those who were studied. There was a history of angina pectoris, developing in the previous nine months, in one subject, and he was given a provisional dyspnoea grading according to his performance before the onset of angina. Another miner had been found to be suffering from myxoedema and was under treatment with thyroid gland extract. His E.C.G. showed evidence of myxoedema but he was not in heart failure.

An E.C.G. record was obtained, as part of the general assessment, in 49 of the 52 miners. There was evidence of ischaemic heart disease in 6, and in 4 of these a former myocardial infarct was suspected. At first this seems rather a high incidence but, in fact, it probably does no more than represent the frequency of myocardial ischaemia in males of this age group. Thomas, Cotes and Higgins (1956) suspected a high incidence of coronary artery disease in South Wales miners. They studied a random sample of miners in the 55 to 64 age group and found that the incidence of coronary disease was 38%. As the mortality rates for coronary disease in coalminers were similar to those for males in other occupations in England and Wales, they considered that the high prevalence rate in miners might not be exceptional for all males in this age group.

The occurrence of the vertical heart pattern on the

E.C.G. has been considered a prelude to the development of right ventricular hypertrophy (Thomas, 1955). In this study, although the vertical heart pattern occurred in 14 of the 44 records, right ventricular hypertrophy was only seen once. Thomas points out that an enlarging left ventricle may obscure the picture of right ventricular hypertrophy, but as no recorded diastolic pressure was above 105 mmHg and there was no evidence of heart failure, this is an unlikely explanation.

Radiological categories.

The numbers in the different categories are seen in Table VI. Category B+ includes category C and D because the numbers were insufficient to support separate groups for analysis. The details of those in category B+ can be seen in the appendix tables.

Miners in category A were not included by Gilson and Hugh-Jones in their study, presumably because of the indefinite nature of the category and the likelihood that it would reduce the discriminatory powers of the respiratory function tests. Category A always occurs on a background of simple pneumoconiosis of category 2 or 3. If the background of simple pneumoconiosis influences the results of a particular test, difficulty will be experienced in demonstrating a regular trend in mean values from the earlier to the later stages of the disease if category A is included in the sequence. Of the 11 miners in category A, six had a background of category 2 simple pneumoconiosis, and five a background of category 3.

There are only four miners with uncomplicated pneumoconiosis of category 3 and their results in some tests are similar to those in category B+. It is possible that these four miners in category 3 were unusually disabled, but that is not apparent either from their subjective dyspnoea grading (dyspnoea grades 2 and 3) or from the objective test of ventilatory capacity (mean Ind. M.B.C. = 91 L/min: range 78 to 105 L/min).

The general radiological appearances have fitted into the accepted international classification without difficulty and there has been nothing to suggest a different dust pattern in these Fife miners.

1. The diffusing capacity

Principles and methods of measurement, choice of test, sources of error.

The rate of diffusion of any gas into a liquid depends directly on its solubility and indirectly on its density. If a membrane is interposed, the characteristics of the membrane also influence the rate of diffusion. In the dynamic situation within the lungs, the rate of diffusion depends on the same factors but the fluid into which the gas is diffusing is capillary blood which is constantly being replaced. If the gas concerned is highly soluble in capillary blood, the rate of transfer is mainly influenced by the pulmonary membrane, but if the gas is much less soluble, the rate is also influenced by the amount of blood flowing through the capillaries. The two gases which are known to be highly soluble in capillary blood, by virtue of their chemical combination with haemoglobin, are oxygen and carbon monoxide. Thus if either of these is used as a test gas, the rate of uptake within the lungs is considered to be influenced primarily by the characteristics of the pulmonary membrane. It is usual to express this rate in terms of millilitres of gas that can be taken up per minute, per mm Hg pressure gradient between alveolus and capillary blood. This is the diffusing capacity of the lungs. It is not a fixed value since it varies with exercise and the method of measurement, and therefore, the conditions of the test should be stated.

The pulmonary membrane is the tissue between the alveolar gas and capillary blood. It has an area and a thickness and both these dimensions may be altered in different ways. The total area available for diffusion is reduced if there is destruction of the normal alveolar architecture or if there is obliteration of the pulmonary capillaries. If the alveoli are normal and the capillaries are perfused, the effective area may be reduced if the airways are obstructed so that inspired gas does not reach the area. The thickness of the membrane may be affected by an exudate of cells or fluid, an abnormal proliferation of cells or the deposition of foreign material anywhere in the diffusion pathway. There is no method by which the membrane surface area and thickness can be measured separately, and the diffusing capacity is only a general expression of the effectiveness of the membrane.

In recent years there has been renewed interest in the diffusing capacity and many techniques have been developed for its measurement.

Because oxygen is a physiological gas, its use in the measurement of the diffusing capacity of the lungs would be preferred to that of carbon monoxide if it were not for considerable technical difficulties. In calculating the amount of gas taken up per mm Hg pressure gradient, it is necessary to know the mean pressure on both sides of the pulmonary membrane. The difficulties in obtaining the mean alveolar gas tension of O_2 and CO are similar but, whereas the mean CO tension in the pulmonary capillaries is so small that it can be neglected, the mean capillary O_2 tension is appreciable and must be calculated. This is a formidable procedure which necessitates the measurement of O_2 tension in arterial blood both when the subject is breathing air and a low level of oxygen mixture of about 12 to 14%. When the subject is breathing air, the O_2 tension gradient between alveolus and arterial blood is made up of 2 components (1) the alveolar to end-capillary gradient due to incomplete equilibration O_2 tension across the pulmonary membrane and (2) end-capillary to arterial gradient due to contamination of arterial blood by venous blood going through the physiological shunt. When a subject breathes a low oxygen mixture, the second of these components is greatly reduced and the first is increased. By this ingenious method of Lilienthal, Riley, Proemmel and Franke (1946) the data necessary for calculating the diffusing capacity of the lungs for O_2 may be obtained.

It is hardly surprising that this method for calculating the diffusing capacity of the lungs has not been used on a wide scale in the study of pneumoconiosis. The principles, however, have been applied by Motley, Lang and Gordon (1950). They used the technique of high and low level O_2 administration to investigate the alveolar to arterial gradient in 50 Pennsylvanian coal-miners suffering from pneumoconiosis. They did not calculate the diffusing capacity for oxygen but make a general statement that the alveolar to arterial O_2 tension gradient was reduced when the subjects breathed 11 to 18% O_2 and increased when they breathed 25 to 27% O_2, thus indicating an upset in ventilation and perfusion ratios rather than a diffusion defect of the pulmonary membrane. This statement may be valid, but insufficient data are given to enable calculations of the diffusing capacity to be made. Mean values for the oxygen "transfer" gradient are given but this gradient, in fact, is the alveolar to arterial gradient with the subject breathing room air and therefore both the membrane and venous admixture components are included. They also report a drop in arterial saturation on exercise which correlated well with the degree of emphysema, and they attribute this to inequality of ventilation and perfusion rather than to a diffusion defect. In some non-emphysematous subjects a drop in arterial saturation also occurred on exercise and this was likewise attributed to a distribution defect. Since the authors relate their findings to the degree of emphysema which is arbitrarily based on the ratio of the residual volume to total lung capacity, little information can be obtained about disordered function in relation to the radiological stage of the disease.

Although carbon monoxide is not a physiological gas, there is no reason to suppose that its diffusion across the pulmonary membrane differs from oxygen. Because of differences in solubility and molecular weight the diffusing capacity for O_2 should, theoretically, be 1.23 times that for CO. Variations in technique may give rise to greater differences and it is probably wise to relate results to the normal values for the actual gas used.

Techniques for measuring CO diffusion are multiple but the main division is into steady state and breath-holding methods.

Steady state methods

When a subject starts to breathe a low concentration of CO, after about 20 breaths the inspired CO is no longer diluted by the CO-free air that was in his lungs before he started. Thereafter the drop in CO concentration between inspired and expired gas is due solely to diffusion into the blood and the subject is said to be in the steady state.

1. The percentage uptake of CO is the most simple of the steady state measurements. In this method, which was introduced by Bates (1952), the volume of CO taken up per minute is calculated from the concentrations of inspired and expired gas and minute volume, and is expressed as a percentage of CO extraction from the inspired gas. Since no allowance is made for the dead space, the percentage extraction diminishes to zero as the tidal volume becomes more and more shallow. Similarly, if ventilation increases to the other extreme and the alveolar concentration of CO is maintained at a high level, diffusion fails to lower alveolar concentration significantly and the percentage extraction is again low. Somewhere between these extremes the percentage extraction is maximal, but the measurement is difficult to standardise because of the dependence on ventilation.

Gilson and Hugh-Jones used this method in their study of pneumoconiosis but increased the efficiency of the measurement by taking post dead space samples of the expired gas. Their index of diffusion was $\frac{\text{inspired CO conc. - alveolar CO conc.}}{\text{inspired CO conc.}}$ and by eliminating the dead space effect they obtained systematically higher values than Bates. Although this index is independent of the dead space/tidal volume ratio, it is still dependent on alveolar ventilation. However Gilson and Hugh-Jones did not find a significant correlation between minute ventilation and percentage CO uptake. They show a scatter diagram in which CO uptake is plotted against ventilation in all subjects, including normals and miners with pneumoconiosis, and certainly there is no obvious correlation. If, however, only those whose percentage CO uptake is below normal (55%) are examined, there is a much wider range of ventilation and, although there is still no obvious correlation, it is more difficult to be sure of the separate effects of increasing ventilation and pneumoconiosis.

Hyperventilation may either be a genuine feature of the disease or the result of the subject's nervousness during the test. Motley, Lang and Gordon (1949) found that hyperventilation was consistently present in the 100 cases of anthracosilicosis which they studied. Rossier, Bucher and Wiesinger (1947) also found a consistent rise in minute volume with each radiological stage, but they point out that this results from an increase in respiratory rate and that the alveolar ventilation remains surprisingly constant. Gilson and Hugh-Jones (1955) confirm this, but also note an increased ventilatory requirement during exercise which they suspect is due to the same causes which impair CO uptake.

In a recent assessment of the steady state methods, MacNamara, Prime and Sinclair (1959) emphasise the difficulty of interpreting the results of the percentage CO uptake if the subject is hyperventilating. Forster, Cohn, Briscoe, Blakemore and Riley (1955) compared the different methods for measuring diffusion and found that the percentage uptake of CO was a more variable index than DL_{O_2} or DL_{CO} measured by either the steady state or breath-holding methods. Forster (1957) concluded that there was little to be gained by measuring the fractional uptake of CO or some variant of it, if the actual diffusing capacity (DL_{CO}) can be measured with little extra trouble.

The various techniques for measuring DL_{CO} by steady state methods revolve round the problem of obtaining the mean alveolar CO tension and the different approaches to this problem are discussed next.

2. By assuming a value for the dead space and by measuring the concentration of the inspired and expired gases, it is possible to solve an algebraic equation for the composition of alveolar gas. This is the Bohr equation which may be solved for any gas, and it states simply that, volume of expired gas = volume of alveolar gas portion + volume of dead space portion.

The main drawback of this method is that at ordinary tidal volumes it is very sensitive to the wrong choice of dead space value. It is much more reliable on exercise when the dead space/tidal volume ratio is reduced as a result of deeper breathing.

If the measurement is done at rest and the subject also suffers from a respiratory disease, the arbitrary choice of a dead space value is not justified.

3. By the method of Bates, Boucot and Dormer (1955) end tidal samples of expired gas are taken by an automatic sampling device and it is claimed that they are representative of alveolar gas. This is probably true for a normal subject with even ventilation of the lungs, provided that the tidal volume is large enough to avoid contamination of the sample by dead space gas. In subjects with uneven ventilation, Marshall (1958) has

shown that this sample is far from representative of alveolar gas. In his experiment, an emphysematous subject breathed a gas mixture containing CO until a steady state was reached. The subject then expired fully into a long tube and gas samples were taken at varying distances from the mouth. Different concentrations of CO were obtained all along the tube, the concentrations rising as the distance from the mouth increased. An end tidal sample is equivalent to a sample taken far from the mouth and is therefore an overestimate of the mean alveolar concentration.

Thus, although this method of measuring DL_{CO} in the steady state is satisfactory for normals, in subjects with uneven ventilation a low result represents a combined ventilatory and diffusion defect. It is not surprising therefore that Bates, Knott and Christie (1956) found that DL_{CO}, measured this way, was useful for assessing disability and prognosis in emphysematous subjects.

In addition to measuring the percentage uptake of CO, Gilson and Hugh-Jones (1955) calculated DL_{CO}, in a few of their subjects, by an ingenious method. They added helium to the usual mixture of CO and air and measured the expired alveolar concentrations of both gases starting from the first breath. The rate of increase of the alveolar He concentration depends on the ratio alveolar ventilation/alveolar volume. The rate of increase of alveolar CO concentration depends on this ratio also, but it is reduced by diffusion which is going on simultaneously (alveolar ventilation - DL_{CO}/alveolar volume). By measuring the two rates and the alveolar volume, they were able to calculate DL_{CO}. However, the stumbling block remains, since the method of obtaining an alveolar sample is the same as that of Bates and therefore, is subject to the same errors.

4. By the method introduced by Filley, MacIntosh and Wright (1954), the mean alveolar CO tension is calculated from a measurement of arterial CO_2 tension and the use of the alveolar air equation. The assumptions are that the partial pressure of CO_2 in arterial blood is equal to the mean alveolar partial pressure of CO_2 and that the dead space for CO and CO_2 are equal. This method requires an arterial puncture and an accurate measurement of the CO_2 tension in arterial blood and thus its use is limited and measurements cannot be repeated easily. Since under-ventilated but perfused areas cause a rise in the partial pressure of CO_2 in arterial blood, DL_{CO} calculated by this method includes an area of lung which only has limited value for gas transfer. It includes all potentially

useable lung and because of this the values obtained in emphysematous subjects tend to be higher than those obtained by the other steady state methods.

Breath-holding method

In addition to measuring CO uptake under steady state conditions, it is possible to measure the rate of uptake by measuring the change in alveolar CO concentration when the breath is held for a known period of time. This method was developed by Krogh (1915) and the procedure was to take two alveolar samples, one immediately after inspiring the CO mixture and the second after the breath holding period. The first sample represented the initial CO concentration at the start of breath holding and the second, the concentration at the end of breath holding. An equation was derived describing the alveolar CO concentration as a function of time from which it was possible to calculate DL_{CO}.

$$\text{alveolar PCO} = \text{initial alveolar PCO} \times e^{-\frac{DL_{CO}\,(B-47)t}{\text{alveolar volume}}}$$

This remained the classical method until Fowler (Forster, Fowler, Bates and Van Lingen, 1954) made the ingenious suggestion of adding 10% helium to the inspired gas mixture. Since He is inert and insoluble, on inspiration it undergoes dilution only and the difference between the inspired and expired concentrations is due solely to this. It is argued that CO is diluted in exactly the same proportions and, therefore, the correct initial alveolar CO concentration can be calculated from the He dilution ratio. Thus the first alveolar sample of the Krogh method is no longer necessary.

The basic assumption of this modification is that there is no process within the lung that separates CO from He except the diffusion of CO into the blood. The calculation of DL_{CO} contains the additional implication that the collected gas sample is representative of the whole lung.

The technical details of the single breath test, which is the one used in this study, have already been given. Like the other tests of diffusion it is not free from sources of error. Some of these have been discussed already and will only be briefly mentioned. Others will be discussed more fully.

1. In all the CO methods the mean capillary tension is considered to be so small that it may be neglected in calculating the pressure gradient. If, for some reason, there is an appreciable amount of COHb in venous blood the diffusion of CO across the pulmonary membrane is

impeded because a certain plasma CO tension exists in equilibrium with the COHb. Significant amounts of COHb may interfere with the test if recirculation occurs before the measurements are completed but this is not a problem with a breath holding time of 10 seconds.

In the extreme case of a heavy smoker who might have as much as 10% COHb in his blood, Ogilvie et al. (1957) have calculated a possible error of 8% in the measurement of DL_{CO}. In practice, McGrath and Thomson (1959) were unable to find any difference between the results of smokers and non-smokers in normal subjects and it is generally agreed that a correction is unnecessary unless the measurement of DL_{CO} is made, for a specific purpose, in the presence of a high alveolar O_2 tension.

In this study the subjects did not smoke within 1 hour of the test. Differences were found between the mean values of the different smoking groups but no regular trend was apparent. The additional factors of age and X-ray category were also operating between the groups and it is much more likely, in view of the evidence of McGrath and Thomson, that differences arose through these rather than through significant levels of COHb in the blood of smokers. The non-smokers, for instance, who had the highest mean value for DL_{CO} were mainly in the early X-ray categories, and smokers in group S2/3, which includes all the miners in the youngest age group, have a higher mean value than those in group S1.

2. The measurement of the duration of breath-holding may be in error if the time of collecting the alveolar sample is prolonged. The error is only significant in subjects whose expiratory flow rate is severely impaired. By restricting the alveolar sample to the 300-400 ml required for gas analysis this error can be kept to a minimum.

3. Provided that the first 750 ml of expiration is discarded, Ogilvie et al. (1957) claim that it does not greatly matter which portion of alveolar gas is used to measure DL_{CO}. A measurement of the volume expired before the sample was taken was made in every test and this was always more than the 750 ml required to wash out the dead space (Fowler, 1949). The He concentration in the sample varies according to whether it is taken early or late and an automatic correction is made in calculating the initial alveolar CO concentration. Thus if the sample is taken from an area of lung that received little of the inspired gas, the He dilution will be greater and the calculated alveolar CO concentration is correspondingly less. Marshall (1958) has shown that DL_{CO} is constant

if calculations are made from different fractions of the alveolar gas even in the presence of severe emphysema. This contrasts with the findings in the method of end tidal sampling which overestimates the mean alveolar CO concentration and under-estimates DL_{CO}. The independence of the breath-holding method from uneven distribution of inspired gas, favours its choice in the measurement of DL_{CO} when it is desired to assess the pulmonary membrane with as little interference as possible from the consequences of complicating emphysema. It is appreciated, however, that in the extreme, impaired alveolar ventilation or blood flow to an alveolus is indistinguishable from impaired diffusion within the alveolus.

Apart from uneven distribution, the question arises as to whether the alveolar sample is representative of the whole lung in regard to diffusing capacity. The early portions of the expiration probably come from better ventilated alveoli than the later portions and it might be expected that they also come from regions of varying diffusing capacity. To investigate this Ogilvie et al. (1957) collected alveolar gas samples after 1000 ml and 2500 ml had been expired and found, in both normals and emphysematous subjects, that DL_{CO} calculated from the later samples was about 10% greater than the earlier. They did not, however, correct for the time taken to deliver the later sample, whereas Marshall, who repeated a similar experiment, did and found that DL_{CO} was uniform throughout expiration. This suggests that any collected alveolar sample is representative of the whole lung.

4. The effect of varying the lung volume at which DL_{CO} is measured is generally agreed to be important (Ogilvie et al., 1957; Marshall, 1958; McGrath and Thomsom, 1959; Donevan et al., 1959). Marshall found that an increase in lung volume of 56% could increase DL_{CO} 24% and this order of increase has been found by others. The difference in normal values obtained by the steady state and single breath methods can largely be explained by differences in lung volume, since the steady state measurement is made with the subject breathing quietly and the lung volume at mid-capacity, and the single breath measurement is made with the subject at, or near, his total lung capacity. In emphysematous subjects the results obtained are commonly higher with the single breath measurement than with the steady state, but part of this may be explained by the different methods of obtaining the alveolar CO concentration.

The steady state method of Filley et al. (1954) most nearly approaches, in results, the single breath method in emphysematous subjects and indeed if a correction is made for the different volumes at which the tests are measured, the results are very similar (Marshall, 1958).

The alveolar volume which is used in the equation for calculating DL_{CO} by the single breath method, is obtained by adding the inspired volume to the residual volume previously measured. This is said by some to be too large, since it includes areas which receive little of the inspired gas. The measurement, in fact, is one of the potential diffusing capacity, rather than the effective diffusing capacity, of the lungs and it does not necessarily represent the ability of a patient, with gross inequality of ventilation, to take up oxygen. It does, however, provide a useful measure of the diffusing capacity of the pulmonary membrane and in the present investigation this is considered to be an advantage since it is desired to assess the separate functions of ventilation and diffusion.

In this study a significant relationship between the total lung capacity and diffusing capacity has been found, and, in examining the relationship between DL_{CO} and the variables of age and X-ray category, it might seem desirable to recalculate DL_{CO} for a standard volume. This, however, is considered to be an over correction because the loss of lung volume, from accumulating dust and tissue reaction, is probably one of the mechanisms by which DL_{CO} itself is reduced.

It is concluded that there are no important theoretical objections to the measurement of the diffusing capacity of the lungs, by the single breath CO method. The method is relatively unaffected by inequality of ventilation and this is considered to be an advantage, since an independent assessment of ventilation and diffusion in pneumoconiosis is desired. The test is rapid and easily repeatable. The reproducibility is at least as good as the other methods and in this study the coefficient of variation within tests on the same subject is 7.3%.

Results

If all the miners in this study are considered together, significantly more than might be expected from chance, have values for DL_{CO} which are below the normal. However, since the effect of age is not taken into account in the prediction of the normal values, it would be premature to claim that pneumoconiosis affects the diffusing capacity. The predicted values of McGrath and Thomson (1959) do take age into account, but unfortunately cannot be used because the different method of calculating the alveolar volume introduces a systematic error. Normal values from other sources are, likewise, inapplicable because the differences in the methods of measurement are even greater.

Effect of age. Within this study, significant differences have been found between the mean values for the different age groups. Roughly, there is a fall in DL_{CO} of 3 to 4 ml/min/mmHg for each 10 year period, as the age rises from 40 to 70. It is difficult to know if this is purely, or even mainly, the effect of age, since, from the nature of the disease, there is a tendency for the older miners to have more dust in their lungs. Most authors are now generally agreed that age affects the results in normal subjects (Cohn et al., 1954; Shepherd, 1958, 1959; McGrath and Thomson, 1959; Donevan et al., 1959) and various mechanisms have been suggested. There may be a reduction in the surface area available for diffusion as a result of changes in the calibre or numbers of pulmonary capillaries, or as a result of degenerative changes in the alveoli. The diffusing capacity is known to rise on exercise and this has been attributed to an expansion of the pulmonary capillary bed consequent upon an increase in cardiac output. Since DL_{CO} by the single breath method is measured at rest, any reduction with age could only be explained, on this basis, by a parallel reduction in the resting cardiac output. Brandfonbrener, Landowne and Shock (1955) have, in fact, reported a reduction in the resting cardiac index with increasing age.

Gilson and Hugh-Jones (1955) give values for the fractional uptake of CO which range from 66% in normal subjects about 25 years old, to 55% in subjects about 55 years old. In miners with pneumoconiosis, however, the tendency for CO uptake to be reduced by advancing age was slight and the differences were not significant.

Since there is no reason to believe that miners with pneumoconiosis escape the consequences of the ageing process, it is considered that the deterioration with advancing age, seen in this study, is genuine.

Effect of X-ray category. Although significant differences between the mean value for DL_{CO} in the different X-ray categories have been established the downward trend with increasing category is irregular.

It may be that it is wrong to regard the change from category 1 simple pneumoconiosis to category B+ complicated pneumoconiosis, as a continuous process. If the "two disease" theory is correct and progressive massive fibrosis (P.M.F.) is a reaction of lungs containing coal dust to a tuberculous infection, then, the radiological sequence is discontinuous and there is no reason to expect a regular trend in the mean values. On the other hand, if P.M.F. is due to the coalescence of dust foci within the lungs, then, the more numerous the foci the more likely is coalescence and the more rational the radiological sequence. However, even if the "two disease" theory is accepted, it is generally agreed that P.M.F. only occurs on a background of category 2 or 3 simple pneumoconiosis or, in other words, when there is sufficient coal dust in the lungs to modify their reaction to a tuberculous infection. Thus, the arrangement of the radiological categories is at least partly justified, but since the background of simple pneumoconiosis varies it is not surprising that irregularities occur between the mean values.

From category 1 to 3 simple pneumoconiosis the downward trend in DL_{CO} is regular. Within category A, significant differences have been demonstrated between those who have a background of category 2 and category 3 simple pneumoconiosis. This partly accounts for the fact that the mean value for category A is higher than that for uncomplicated pneumoconiosis of category 3. The mean value for those with category B or worse, is very similar to the mean value for category 3. Category B+ also contains those with background categories 2 and 3, but in contrast to category A, the areas of massive fibrosis are increasingly important in influencing the individual results. In fact category B+, in terms of pathology, covers too wide a span for the mean value to have any absolute significance.

The differences between the different X-ray categories are not explained by variations in size of the subjects because, when the diffusing capacity is expressed as a percentage of the normal value, the differences are still significant ($P < 0.01$). It is not possible to eliminate the variation due to age in the X-ray categories, by expressing the results as a percentage of the normal. However, since the differences between the X-ray categories are more significant ($P < 0.01$) than the differences between the age groups ($P < 0.05$), it is apparent that the effect of age is only partial.

In contrast to the results in this study, Gilson and

Hugh-Jones report hardly any change in CO uptake between the categories of simple pneumoconiosis. They found a decrease of 30% in those with advanced pneumoconiosis of category C and D, and compared with all the other categories this was significant. They argue that their method was capable of detecting a diffusion defect because low results were obtained in two patients suffering from pulmonary fibrosis due to other causes. However, even in their most advanced cases of pneumoconiosis the reduction in CO uptake was comparable with that seen in severe cases of emphysema rather than with the cases of pulmonary fibrosis.

The single breath test has been more successful in detecting differences between the categories and the absolute values obtained in many cases (see Figure 13), are comparable with those obtained in patients who have well established pulmonary fibrosis due to other causes.

Mechanisms for reduction in diffusing capacity in pneumoconiosis

The consequences of inhaling dust into the lungs depend on how much inhaled dust is retained in the lungs and the tissue reaction of the lungs to it. Detailed analysis of the lungs of deceased coal miners for coal, total silica, quartz, kaolin and mica, have been made by chemical and X-ray defraction methods by King, Maguire and Nagelschmidt (1956). They found an average value of 35 G of total dust, including 0.9 G of quartz, in the lungs of colliers and this probably represented an accumulation of 1 G of dust per year of occupation. The amount of dust increased with each of their pathological grades which were those of reticulation, mixed nodulation and confluent fibrosis. The relative amounts of coal dust and quartz varied with different occupations in the mines, the rock workers having less coal and more quartz than the colliers and hauliers.

The early changes brought about in the lung have been described in detail by Heppleston (1947, 1954) and Gough and Heppleston (1955). Whole lung sections show dust foci scattered uniformly throughout and histological preparations show deposits of dust-laden macrophages enmeshed in a reticular frame work and forming cuffs around the respiratory bronchioles. Collagen fibres within the foci are scanty until complications develop. Often, and more frequently with increasing age, the foci are surrounded by emphysema.

The mixed nodulation referred to by King et al. (1956) appears as small fibrous nodules impregnated with coal dust and containing much collagen. These lesions are usually less than 1.5 cm and there are differences of opinion as to whether the fibrosis is a reaction to silica or to infection. Faulds, King and Nagelschmidt (1959) have reported the histological appearances and dust content of the lungs of coalminers from Cumberland. There, this type of nodulation is more frequent and in addition, each histological grade has less coal and more quartz than the corresponding grades in coalminers from South Wales.

The third main type of lesion is progressive massive fibrosis which consists of a dense mass of collagen containing a large amount of coal dust. The masses vary greatly in size, may be bilateral and are commonly in the upper lobes of the lungs. Bronchi and vessels within the mass are obliterated and vessels at the periphery show advanced endarteritis. The edge of these lesions is irregular and whereas fibrosis is predominantly localised to the mass, linear extensions into the surrounding lung tissue can be seen.

From the description of the main pathological features it is apparent that the diffusing capacity of the lungs can be affected in different ways.

1. By silting up of coal dust within the alveoli, particularly when coal dust has been recently inhaled

and the mechanisms for its removal are defective, the diffusion pathway may be obstructed.

2. By the accumulation of coal dust and phagocytes in and around the respiratory bronchioles, an effective area for gas exchange is lost.
3. By the slowly progressive increase in coal dust foci, mixed nodules and areas of massive fibrosis, the volume of normally functioning lung is reduced and with it the total surface area available for gas exchange.
4. By the involvement of the pulmonary vasculature in or near areas of massive fibrosis, there may be interference with the perfusion of normal alveoli.
5. By the extension of fibrous strands from areas of massive fibrosis, the septal tissues may be thickened in localised areas.

Of these possibilities the one that probably can be accepted most readily is the reduction of normally functioning lung tissue. Although there may only be about 35 G of dust in the lungs, the radiological appearances often convey the impression that the lungs are choked with dust. But radiological opacities are composed of more than dust and tissue reaction to dust must contribute to the appearances and also to the encroachment upon normally functioning lung tissue.

It has been recognised for some time that rock workers in the mines are at greater risk and account for a relatively higher proportion of those with radiological abnormalities than other occupations (Hart and Aslett, 1942). The dust composition of their lungs is also different in that the proportion of quartz is higher (King and Nagelschmidt, 1945) and because of this, nodulation of the silicotic type is more frequent. It is of interest therefore, that in this study it was found that miners who had spent 10 or more years in stone-work had values for the diffusing capacity which were significantly lower than the remainder. Their ventilatory capacity, on the other hand, was not significantly different from the others and therefore it appears that there may be different emphases on disordered pulmonary function in coalminers in different occupations. A single test of ventilatory capacity is consequently an inadequate assessment of the individual.

Relationship to dyspnoea. The most direct way of assessing breathlessness is to question the subject, but there is a risk that the answers may be inaccurate if the subject is suffering from a pensionable disease. Nevertheless this method is preferred to an assessment of breathlessness or disability by a single test of lung function, such as the Ind. M.B.C., because this implies that breathlessness is due to impairment of this function only.

In this study DL_{CO} correlated poorly with Ind. M.B.C., but there was a significant relationship between the diffusing capacity and dyspnoea. There is a fall in the mean values for DL_{CO} with increasing dyspnoea grade, and if the variation due to body size is eliminated by expressing DL_{CO} as a percentage of the predicted normal value, the relationship to dyspnoea is statistically significant (see Figure 12, page 55).

Since DL_{CO} is significantly related to dyspnoea its measurement is of clinical interest. By calculating the diffusing capacity of the lungs for oxygen indirectly ($DL_{CO} \times 1.23 = DL_{O_2}$), it is possible to estimate the mean O_2 pressure gradient which the subject must maintain to supply his resting O_2 requirements. For instance, if DL_{CO} = 20 ml/min/mmHg, $DL_{O_2} = 20 \times 1.23 = 24.6$ ml/min/mmHg: if O_2 requirements = 246 ml/min, then mean O_2 pressure gradient between alveolus and capillary blood = 10 mmHg. A gradient of this order is normal and should not give rise to dyspnoea at rest.

For practical purposes, however, diffusion assumes greater importance during exercise, because, as a result of an increase in the velocity of blood flowing through the capillaries, there is less time for gas transfer. From the point of view of clinical significance, there is no single critical level for DL_{CO} since any such level varies with the oxygen requirements at different levels of activity.

Gilson and Hugh-Jones found a correlation between the percentage uptake of CO and a clinical grading of dyspnoea ($r = 0.428$). It was, nevertheless, one of their tests which correlated least well with dyspnoea, but when it was related to the ventilatory requirements on exercise a clear inverse relationship was seen. An increased ventilatory requirement on exercise was noted in their more advanced pneumoconiotics and it correlated poorly with inequality of gas distribution. They concluded therefore, that it was not due to emphysematous changes in the lungs but more probably to the same factors which impair the uptake of CO. These findings are not incompatible with the ones in this study and they support the view that a lowered diffusing capacity in miners with pneumoconiosis may aggravate their disability by increasing the ventilatory requirement on exercise.

Relationship to chronic bronchitis and smoking. No significant relationship between the diffusing capacity and chronic bronchitis has been demonstrated in this study but in view of the lower mean value of the bronchitics as compared with the others, no final conclusion should be drawn. It is difficult to imagine how bronchitis can affect the pulmonary membrane except by reducing the effective surface area. Intraluminar secretions could effectively cut off small areas, particularly if the secretions lay across the mouths of the subdivisions of the smaller bronchi. The surface tension of such bubbles may be very considerable and the interruption of ventilation may be complete.

The relationship of the diffusing capacity to smoking is likewise dubious. Except as a result of the presence of significant amounts of COHb in the blood of smokers, there are no obvious reasons for a reduction in the diffusing capacity. This possibility has been discussed already and it is not believed that it offers a satisfactory explanation for the differences within the smoking groups. The differences are irregular and it is felt that they are probably due to factors other than smoking, operating within the groups.

<u>Relationship to other tests</u>. The importance of the lung volume in relation to the results obtained by the different methods of measuring the diffusing capacity have been discussed. Even when using the same method, a relationship between DL_{CO} and the lung volume has been found in this study. This is not surprising, because in normals it has been found that bigger men have larger diffusing capacities. In pneumoconiosis there is an additional reason, since dust and tissue reaction gradually encroach upon normal tissue and reduce both the lung volume and the effective area for diffusion. The effects are inseparable and, therefore, no attempt has been made to standardise DL_{CO} for lung volume.

No significant relationship has been found between the diffusing and ventilatory capacities. It seems likely, therefore, that the functions of ventilation and diffusion are not affected in parallel. Variations in the type of pulmonary disorder are to be expected because miners are subject to non-industrial diseases such as bronchitis and emphysema, in the same way as the general population. Varying tissue responses by the host to coal dust have been postulated (Vigliani and Pervis, 1958) and it may be that fibrous tissue and collagen are provoked more readily in some. The effects of dust of varying composition inhaled by miners in different underground occupations have already been discussed. The possibility exists, therefore, of a selective impairment of either the ventilatory or diffusing capacities and that being so, a lack of correlation between them is not surprising.

A relationship between the diffusing capacity and compliance has not been established. Compliance and DL_{CO} both tend to decrease along with the lung volume, and the pathological changes which have been postulated to explain the reduction in DL_{CO} might also affect compliance. Further investigation of the relationship between the two measurements is desirable since, although there is no significant correlation, the actual values are suggestive.

2. Ventilatory function

The popularity of the maximum breathing capacity, or some variant of it, for assessing pulmonary disability is due to its ease of measurement, repeatability and high correlation with symptomatology. In the common chronic lung diseases, such as asthma, bronchitis and emphysema, it is particularly useful since the ventilatory function of the lungs is especially impaired. In miners with pneumoconiosis, it is no less useful and Gilson and Hugh-Jones found a high correlation between the maximum voluntary ventilation and an independent assessment of dyspnoea ($r = 0.77$).

Using the Ind. M.B.C., a highly significant correlation with a subjective dyspnoea grading has been obtained in this study ($F = 6.4$, $P < 0.01$). It is readily agreed that there may be other causes of dyspnoea than an impaired ventilatory capacity but the test is so well established that a relationship of this order implies that the dyspnoea grading is accurate.

The relation of the ventilatory capacity to the radiological stage of pneumoconiosis is less apparent. There is general agreement that the ventilatory capacity is lowered in complicated pneumoconiosis (Gilson and Hugh-Jones, 1955; Higgins, Oldham, Cochrane and Gilson, 1956; Lethart, 1959), but in simple pneumoconiosis the changes are slight. Thus Lavenne and Belayew (1953) found no change in simple pneumoconiosis: Carpenter et al. (1956) found lower average values as the categories increased from 1 to 3 but they remark on the wide scatter within each category: and Lethart (1959) actually found higher mean values for those in category 2 than category 1 and no significant differences between categories 1, 2 or 3.

The findings in this study are similar, since although there is a slight fall with increasing radiological category there are no significant differences.

From the radiological appearances of pneumoconiosis, it appears to be easier to draw conclusions about the diffusing capacity than about the ventilatory capacity. This is not surprising because other diseases which are not so apparent radiologically, such as bronchitis and emphysema, often cause a reduction in the ventilatory capacity and the pneumoconiotic miner is not immune from these.

The failure to demonstrate significant differences between Ind. M.B.C. of those with chronic bronchitis and those without, has already been discussed. There is in fact a difference in mean values of 15 L/min but it is not significant ($F = 3.28$, $0.2 > P > 0.05$).

In the 34 subjects in whom compliance was measured, no significant relationship was found with Ind. M.B.C. This is in keeping with the findings of Lethart (1959) who concluded that stiffness of the lungs was not the explanation of a reduced ventilatory capacity when it occurred in pneumoconiosis.

The measurement of non-elastic airway resistance by the method of Mead and Whittenberger (1953) is less informative in subjects who have a marked expiratory resistance, because for technical reasons the measurement can only then be made on inspiration. The inspiratory resistance does not correlate well with measurements of the expiratory flow rate (Lethart, 1959) and is, therefore, of limited value.

In this study the inspiratory and expiratory flow rates have been measured spirometrically and the ratio of the one to the other examined $\left(\frac{\text{M.E.F.R.}}{\text{M.I.F.R.}}\right)$. Previously McNeill et al. (1959) had found a significant correlation between this ratio and dyspnoea in miners with pneumoconiosis, but here, although the ratio falls with increasing dyspnoea the differences are not significant. The explanation is that the proportion of miners with severe dyspnoea was much larger in the former study and the changes in the ratio correspondingly greater. It appears that the ratio is not of great value for comparative purposes if the subjects are not very disabled, but it does help to reveal the nature of the underlying mechanical defect in those who have a severe impairment of the ventilatory capacity.

3. <u>Lung volumes</u>

Measurement of the static lung volumes are generally thought to be of limited value, since they are inferior to the tests of ventilatory capacity in their correlations with disability. Nevertheless since the functions of ventilation, gas mixing and gas transfer all depend on the lung volume and the proportion of it that is exchanged by the tidal volume, the various subdivisions deserve attention.

Early measurements in pneumoconiosis by McMichael (1942), showed a reduction in vital capacity and total lung capacity which was more marked with increasing radiological stage. Because of a wide scatter in the results, however, the measurements were not helpful in individual cases. Motley, Gordon and Lang (1949) studied a large number of miners and found that the vital capacity correlated poorly with the degree of emphysema that was present. However, they arbitrarily defined emphysema according to the ratio of residual volume to total lung capacity, 35% being the upper limit of normal. With this definition, they found a good relationship between $\frac{\text{R.V.}}{\text{T.L.C.}}\%$ and disability but no relationship to the radiological stage of pneumoconiosis. It was hardly surprising that they found cases of severe "emphysema" with minimal radiological changes and vice versa. In a third of their cases there was no increase in $\frac{R.V.}{T.L.C.}\%$ and in these they attributed disability, when present, to inequality of ventilation and perfusion consequent upon pulmonary fibrosis.

Gilson and Hugh-Jones (1955) found a fall in total lung capacity in the more advanced stages of pneumoconiosis which was mainly due to a fall in vital capacity. This is unlike the findings in severe emphysema, uncomplicated by dust disease, where there is an increase in total lung capacity and residual volume and a decrease in vital capacity. They found a slight increase in $\frac{R.V.}{T.L.C.}\%$ with age and X-ray category, the increases being smaller and less frequent than those reported by Motley et al. (1949).

In this study, vital capacity correlates well with age, but when this is allowed for, by expressing the result as a percentage of normal, no differences are seen in either the radiological stages or the dyspnoea grades.

The total lung capacity on the other hand, is significantly different in the various radiological categories and this is not due to age because it persists when the results are expressed as a percentage of normal. The fall in T.L.C. is not restricted to the later categories, but occurs within the categories of simple pneumoconiosis as well. There is no significant correlation between T.L.C. and the degree of dyspnoea and none between T.L.C. and Ind. M.B.C. Any emphysema, due to non-industrial causes, is likely to impair the ventilatory capacity and increase disability. Pneumoconiosis, on the other hand, does not impair the ventilatory capacity until the later stages are reached and it is associated with a progressive fall in T.L.C.

The $\frac{\text{R.V.}}{\text{T.L.C.}}\%$ was found to fall slightly with advancing pneumoconiosis and this is in contrast to Gilson and Hugh-Jones who found a slight upward trend. They did, however, find a fall in absolute values for residual volume except in the most advanced stage.

The relationship between $\frac{\text{R.V.}}{\text{T.L.C.}}\%$ and dyspnoea in this study is suggestive although not significant. There is a rise in mean value with each increase in dyspnoea grade and although this is in keeping with the findings of Motley et al. (1949), it is felt that there is no justification for using the ratio as a measure of disability.

4. <u>Lung compliance</u>

Apart from the work of Lethart (1959) there has been no detailed analysis of the mechanical properties of the lungs in pneumoconiosis. The compliance of the lungs might be affected in this disease as the result of two possible mechanisms; (1) increase in fibrous and elastic tissue due to the fibrogenic action of inhaled dust, (2) reduction in the normal lung volume. The first of these is unlikely in coalminers pneumoconiosis since coal dust is not significantly fibrogenic. The second is likely because a reduction in total lung capacity has been demonstrated and because Marshall (1957) reported a good correlation between compliance and the lung volume. Lethart (1959) did, in fact, find some evidence of a reduced compliance in subjects with P.M.F. but the reduction was slight and a normal value was often obtained. The areas of massive fibrosis appear to influence the measurement little, possibly because it is made during quiet breathing when the relatively normal areas are being ventilated.

In this study no significant relationship was found between compliance and age, X-ray category or disability. A significant relationship was found with the functional residual capacity and total lung capacity, which is in keeping with the findings of Marshall (1957) in normals. It may be that the size of the subject is a more important influence, in this relationship, than the reduction in volume due to disease.

Compliance was measured in a relatively small number of the subjects and consequently significant relationships are more difficult to demonstrate.

5. Blood findings

Although all the blood indices were measured, only the haemoglobin levels are quoted in the results. The changes in red cell count and packed cell volume parallelled the changes in haemoglobin and do not therefore offer any additional information. The white cell counts were all within the normal range and there was no evidence that those who suffered from chronic bronchitis had higher values.

There is agreement that polycythaemia, or a rise in haemoglobin level, is rare in pneumoconiosis (Motley et al., 1950; Gilson and Hugh-Jones, 1955). This is so even in the more advanced stages even where arterial unsaturation is present.

Anaemia likewise, is uncommon and chronic bronchitis was found to have no effect here in lowering the haemoglobin level.

Because the mean haemoglobin levels in the various subgroups are all within the normal range, the finding of significant differences between the groups is of little clinical importance. Thus there is a minor fall in haemoglobin with increasing age and X-ray category. The fall with increasing dyspnoea is reversed in the worst grade and since a similar change in venous CO_2 content occurs in this grade, there may be a physiological explanation for it. Quantitatively, however, the change is insignificant.

In addition to confirming the relative stability of the haemoglobin level in pneumoconiosis, its relationship to the diffusing capacity is of interest. For theoretical reasons which have been mentioned previously, the diffusing capacity is influenced by the amount of haemoglobin lying in the pulmonary capillaries. If there is no compensating change in pulmonary capillary blood volume, the diffusing capacity should be low in anaemia. This has been confirmed by Rankin, McNeill and Forster (1957) who found a 50% reduction in diffusing capacity in severely anaemic patients with an average haemoglobin value of 6 G%. As the anaemia was corrected, the diffusing capacity returned to normal. Thus, in any wide scale study of the diffusing capacity it is important to establish that the haemoglobin levels are not influencing the results.

The CO_2 content of venous blood is not generally regarded as a useful measure in chronic pulmonary disease. Like haemoglobin, the mean values for the various subgroups are within the normal range with the exception of the worst dyspnoea grade. Here, the value is significantly higher than in the other dyspnoea grades and the probability is that it reflects the development of CO_2 retention in the most disabled subjects. A metabolic acidosis, associated with hyperventilation and mistaken for dyspnoea, would result in a lowered CO_2 content in the venous blood. In the different X-ray categories the values are normal, but a rise is seen in category B+. This suggests that the increase in ventilation that has been reported in pneumoconiosis, is adequate in the earlier categories but may become inadequate in the later stages.

SUMMARY

1. Fifty-two miners with pneumoconiosis have been studied and their age, disability and radiological appearances described in detail.

2. The nature and severity of the disorder of pulmonary function has been investigated by measurements of -

    (i) The diffusing capacity.

    (ii) The ventilatory capacity.

    (iii) The lung volumes.

    (iv) Lung compliance.

3. It has been found that -

    (i) The diffusing capacity falls with increasing age.

    (ii) The diffusing capacity falls as the radiological stage of the disease advances and this is only partly explained by the effect of age. The fall is irregular, especially in the change from simple to complicated pneumoconiosis. This is mainly due to variation in the background of simple pneumoconiosis in category A.

    (iii) The diffusing capacity falls as breathlessness increases.

(iv) The diffusing capacity is not related to the ventilatory capacity, suggesting that the impairment of each function is separate.

(v) The diffusing capacity falls with the total lung capacity. The loss of normally functioning lung may be one of the mechanisms by which it is reduced.

4. The ventilatory function of the lungs, as measured by the indirect maximum breathing capacity, relates well to the complaint of breathlessness. It does not relate well to the radiological stage of pneumoconiosis.

5. Lung volume estimations show that the total lung capacity is reduced as the radiological stage of pneumoconiosis advances. The ratio of the residual volume to the total lung capacity is not related to the radiological stage, but the average values rise with increasing breathlessness.

6. Measurements of lung compliance, in 34 subjects, show no increase in stiffness of the lungs with advancing radiological disease. There is a general relationship to lung volume, the lungs being less compliant as the functional residual and total lung capacities fall.

Acknowledgements

This work has been generously supported by the Secretary of State for Scotland and the National Coal Board.

Professor R. B. Hunter initially suggested the study of coalminers and by his characteristic energy obtained laboratory facilities and equipment to make it possible. I am very grateful to him for his unfailing enthusiasm.

Drs. H. A. Graham, G. D. Malcolm, and A. Cubie allowed me to study miners under their care. Dr. G. D. Malcolm has been particularly helpful and interested and has provided additional records for study. Dr. J. McLeod and Dr. Stewart Rae interpreted and graded the X-ray films and Dr. H. Watson interpreted the electrocardiographic records. Dr. G. Smith and his staff carried out the haematological studies, except for the Van Slyke analyses which were done by Mrs. Mary Stark (B.Sc.). Mrs. Stark was also my assistant in the pulmonary function laboratory during most of the study. To all these I owe my sincere thanks.

Finally, I wish to thank Dr. W. A. Wilson, medical statistician of the Department of Public Health and Social Medicine, Queen's College, Dundee, for the analysis of the results. He has freely given me his time and invaluable advice.

R E F E R E N C E S

REFERENCES

Bates, D. V., (1952) The uptake of carbon monoxide in health and in emphysema. Clin. Sci. 11, 21.

Bates, D. V., Boucot, N. G. and Dormer, A. E., (1955) The pulmonary diffusing capacity in normal subjects. J. Physiol. 129, 237.

Bates, D. V., Knott, J. M. S. and Christie, R. V., (1956) Respiratory function in emphysema in relation to prognosis. Quart. J. Med. 25, 137.

Bernstein, L., D'Silva, J. L. and Mendel, D., (1952) The effect of the rate of breathing on the maximum breathing capacity determined with a new spirometer. Thorax 7, 255.

Black, J., (1953) Pneumoconiosis of coal miners in Scotland. Brit. J. industr. Med. 10, 101.

Brandfonbrener, M., Landowne, M. and Shock, N. W., (1955) Changes in cardiac output with age. Circulation 12, 557.

Carpenter, R. G., Cochrane, A. L., Gilson, J. C. and Higgins, I. T. T., (1956) The relationship between the ventilatory capacity and simple pneumoconiosis in coalworkers. Brit. J. industr. Med. 13, 166.

Cohn, J. E., Carroll, D. G., Armstrong, B. W., Shephard, R. H. and Riley, R. L., (1954). Maximal diffusing capacity of lung in normal male subjects of different ages. J. appl. Physiol. 6, 588.

Comroe, J. H., Forster, R. E., DuBois, A. B., Briscoe, W. A. and Carlsen, E., (1955) The Lung. Year Book Publishers, Inc., Chicago.

Consolazio, C. F., Johnson, R. E. and Marek, E., (1951) Metabolic Methods. The C. V. Mosby Company, St. Louis.

Craig, W., (1834) Observations on spurious melanosis. Edinb. med. surg. J. 42, 330.

Donevan, R. E., Palmer, W. H., Varvis, C. J. and Bates, D. V., (1959) Influence of age on pulmonary diffusing capacity. J. appl. Physiol. 14, 483.

DuBois, A. B., Britt, A. G. and Fenn, W. O., (1952) Alveolar CO_2 in respiratory cycle. J. appl. Physiol. 4, 535.

Faulds, J. S., King, E. J. and Nagelschmidt, G., (1959) The dust content of the lungs of coal workers from Cumberland. Brit. J. industr. Med. 16, 43.

Filley, G. F., MacIntosh, D. J. and Wright, G. W., (1954) CO uptake and pulmonary diffusing capacity in normal subjects at rest and during exercise. J. clin. Invest. 33, 530.

Fletcher, C. M., Elmes, P. C., Fairbairn, A. S. and Wood, C. H., (1959) Significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. Brit. med. J. 2, 257.

Forster, R. E., Fowler, W. S., Bates, D. V. and Van Lingen, B., (1954) Absorption of CO by the lungs during breath holding. J. clin. Invest. 33, 1135.

Forster, R. E., Cohn, J. E., Briscoe, W. A., Blakemore, W. S. and Riley, R. L., (1955) A modification of the Krogh CO breath holding technique for estimating the diffusing capacity of the lung. J. clin. Invest. 34, 1417.

Forster, R. E., (1957) Exchange of gases between alveolar air and pulmonary capillary blood: pulmonary diffusing capacity. Physiol. Rev. 37, 391.

Fowler, W. S., (1949) Lung function studies. III. Uneven pulmonary ventilation in normal subjects and in patients with pulmonary disease. J. appl. Physiol. 2, 283.

Gandevia, B. and Hugh-Jones, P., (1957) Terminology for the measurement of ventilatory capacity. Thorax 12, 290.

Gilson, J. C. and Hugh-Jones, P., (1955) Lung Function in coalworkers' pneumoconiosis. Spec. Rep. Ser. med. Res. Coun. Lond. No. 290. H.M. Stationery Office.

Gough, J. and Wentworth, J. E., (1949) The pathology of the pneumoconiosis of coalworkers in Wales; a new technique for the study of lung pathology. Proc. 9th Int. Cong. Industr. med. London, 1948 p.661.

Gough, J. and Heppleston, A. G., (1955) Nature 176, 762.

Gregory, J. C., (1831) Case of peculiar black infiltration of the whole lungs, resembling melanosis. Edinb. med. surg. J. 36, 389.

Hall, J. A. M., (1937) A study of chronic chest diseases among coal miners in Shotts, Scotland. J. industr. Hyg. 19, 506.

Hart, P. d'A. and Aslett, E. A., (1942) Chronic pulmonary disease in South Wales coalminers. Spec. Rep. Ser. med. Res. Coun., Lond. No. 243. H.M. Stationery Office.

Heppleston, A. G., (1947) Essential lesion of pneumokoniosis in Welsh coal workers. J. Path. Bact. 59, 453.

Heppleston, A. G., (1951) Coal workers' pneumoconiosis; pathological and etiological considerations. Arch. industr. Hyg. 4, 270.

Heppleston, A. G., (1954) The pathogenesis of simple pneumoconiosis in coal-workers. J. Path. Bact. 67, 51.

Herrald, F. J. C. and McMichael, J., (1939) Determination of lung volume: a simple constant volume modification of Christie's method. Proc. roy. Soc. Med. Series B, 126, 491.

Higgins, I. T. T., Oldham, P. D., Cochrane, A. L. and Gilson, J. C., (1956) Respiratory symptoms and pulmonary disability in an industrial town. Survey of a random sample of the population. Brit. med. J. 2, 904.

Higgins, I. T. T., (1959) Tobacco smoking, respiratory symptoms and ventilatory capacity. Studies in random samples of the population. Brit. med. J. 1, 325.

International Labour Office, (1953) Proceedings of the Third International Conference of Experts on Pneumoconiosis. Sydney, Australia, 1950, Geneva.

Kennedy, M. C. S., (1953) A practical measure of the maximum ventilatory capacity in health and disease. Thorax 8, 73.

King, E. J., Nagelschmidt, G., (1945) Chronic pulmonary disease in South Wales coalminers. Spec. Rep. Ser. med. Res. Coun., Lond. No. 250. H.M. Stationery Office.

King, E. J., Maguire, B. A., Nagelschmidt, G., (1956) Further studies of the dust in lungs of coal-miners. Brit. J. industr. Med. 13, 9.

Krogh, M., (1915) Diffusion of gases through the lungs of man. J. Physiol. 49, 271.

Lavenne, F. and Belayew, D. D., (1953) Report No. 106, Institut d'Hygiene des Mines. Hasselt, Belgium.

Lethart, G. L., (1959) The mechanical properties of the lung in pneumoconiosis of coal-miners. Brit. J. industr. Med. 16, 153.

Lilienthal, J. L., Riley, R. L., Proemmel, D. D. and Franke, R. E., (1946) An experimental analysis in man of the O_2 pressure gradient from alveolar air to arterial blood during rest and exercise at sea level and at altitude. Amer. J. Physiol. 147, 199.

Macnamara, J., Prime, F. J. and Sinclair, J. D., (1959) An assessment of the steady-state carbon monoxide method of estimating pulmonary diffusing capacity. Thorax 14, 166.

McCallum, R. I. and Newell, D. J., (1958) Pneumoconiosis of coal-miners in three Northumbrian collieries. Brit. J. industr. Med. 15, 178.

McGrath, W. M. and Thomson, M. L., (1959) The effect of age, body size and lung volume change on alveolar-capillary permeability and diffusing capacity in man. J. Physiol. 146, 572.

McMichael, J., (1942) Spec. Rep. Ser. med. Res. Coun., Lond., No. 243, p.120. H.M. Stationery Office.

McNeill, R. S. and McKenzie, J. M., (1958) A clinical and spirometric assessment of airway resistance in rheumatic heart disease. Scot. med. J. 3, 417.

McNeill, R. S., Rankin, J. and Forster, R. E., (1958) The diffusing capacity of the pulmonary membrane and the pulmonary capillary blood volume in cardio-pulmonary disease. Clin. Sci. 17, 465.

McNeill, R. S., Malcolm, G. D. and Brown, W. R., (1959) A comparison of expiratory and inspiratory flow rates in health and in chronic pulmonary disease. Thorax 14, 222.

Marshall, R., (1957) The physical properties of the lungs in relation to the subdivisions of lung volume. Clin. Sci. 16, 507.

Marshall, R., (1958) A comparison of methods of measuring the diffusing capacity of the lungs for carbon monoxide. Investigation by fractional analysis of the alveolar air. J. clin. Invest. 37, 394.

Marshall, W., (1834) Cases of spurious melanosis of the lungs or of phthisis melanotica. Lancet 2, 271.

Mead, J. and Whittenberger, J. L., (1953) Physical properties of human lung measured during spontaneous respiration. J. appl. Physiol. 5, 779.

Motley, H. L., Lang, L. P. and Gordon, B., (1949) Pulmonary emphysema and ventilation measurements in one hundred anthracite coal miners with respiratory complaints. Amer. Rev. Tuberc. 59, 270.

Motley, H. L., Lang, L. P. and Gordon, B., (1950) Studies on the respiratory gas exchange in one hundred anthracite coal miners with pulmonary complaints. Amer. Rev. Tuberc. 61, 201.

Meiklejohn, A., (1951) History of lung diseases of coal miners in Great Britain: Part I, 1800-1875. Brit. J. industr. Med. 8, 127.

Needham, C. D., Rogan, M. and McDonald, I., (1954) Normal standards for lung volumes, intra-pulmonary gas-mixing and maximum breathing capacity. Thorax 9, 313.

Nisell, O. I. and DuBois, A. B., (1954) Relationship between compliance and F.R.C. of the lungs in cats, and measurement of resistance to breathing. Amer. J. Physiol. 178, 206.

Ogilvie, C. M., Forster, R. E., Blakemore, W. S. and Morton, J. W., (1957) A standardized breath holding technique for the clinical measurement of the diffusing capacity of the lung for carbon monoxide. J. clin. Invest. 36, 1.

Ogilvie, C., (1959) Patterns of disturbed lung function in patients with chronic obstructive vesicular emphysema. Thorax 14, 113.

Pappenheimer, J. R., Comroe, J. H., Cournand, A., Ferguson, J. K. W., Filley, G. F., Fowler, W. S., Gray, J. S., Helmholz, H. F., Otis, A. B., Rahn, H. and Riley, R. L., (1950) Standardization of definitions and symbols in respiratory physiology. Fed. Proc. 9, 602.

Rankin, J., McNeill, R. S. and Forster, R. E., (1957) Effect of anaemia on pulmonary diffusing capacity. Fed. Proc. 16, 103.

Rossier, P. H., Bucher, H. and Wiesinger, K., (1947) Uber die Silikose III. Studien uber die Pathophysiologie der Atmung bei der Silikose. Vjschr. naturf. Ges. Zurich 92, Beihefte 3-4, p.83.

Roughton, F. J. W. and Forster, R. E., (1957) The relative importance of diffusion and chemical reaction rates in determining the exchange of gases in the human lung with special reference to the volume of blood in the lung capillaries and the true diffusing capacity of the lung membrane. J. appl. Physiol. 11, 290.

Shephard, R. J., (1958) Partitional respirometry in human subjects. J. appl. Physiol. 13, 357.

Shephard, R. J., (1959) Partitional respirometry in cardio-pulmonary disease. Thorax 14, 153.

Thomas, A. J., (1955) Spec. Rep. Ser. med. Res. Coun., Lond. No. 290. H.M. Stationery Office.

Thomas, A. J., Cotes, J. E., Higgins, I. T. T., (1956) Prevalence of coronary heart disease in elderly coal-workers. Lancet 1, 414.

Vigliani, E. C. and Pernis, B., (1958) Immunological factors in the pathogenesis of the hyaline tissue of silicosis. Brit. J. industr. Med. 15, 8.

A P P E N D I X

APPENDIX (1)

Mining environment in the Fife coalfields

The location and subdivisions of the Fife coalfields have been described by Dr. J. Black (1953) and I am grateful to him and to the editor of the British Journal of Industrial Medicine for permission to reproduce the map shown in Figure 33. The subdivisions and colliery areas within them are:-

B1. Clackmannan and West Fife; Clackmannan, Comrie and Valleyfield districts.

B2. Central Fife; Dunfermline, Cowdenbeath and Lochgelly districts.

B3. East Fife; Kirkcaldy, Wemyss and Leven districts.

By far the greater number in this study came from Central Fife (B2).

The Fife coalfield is well developed and mechanised and over 90% of the coal was machine-cut in 1947 which was the highest for any area in Scotland (Black, 1953).

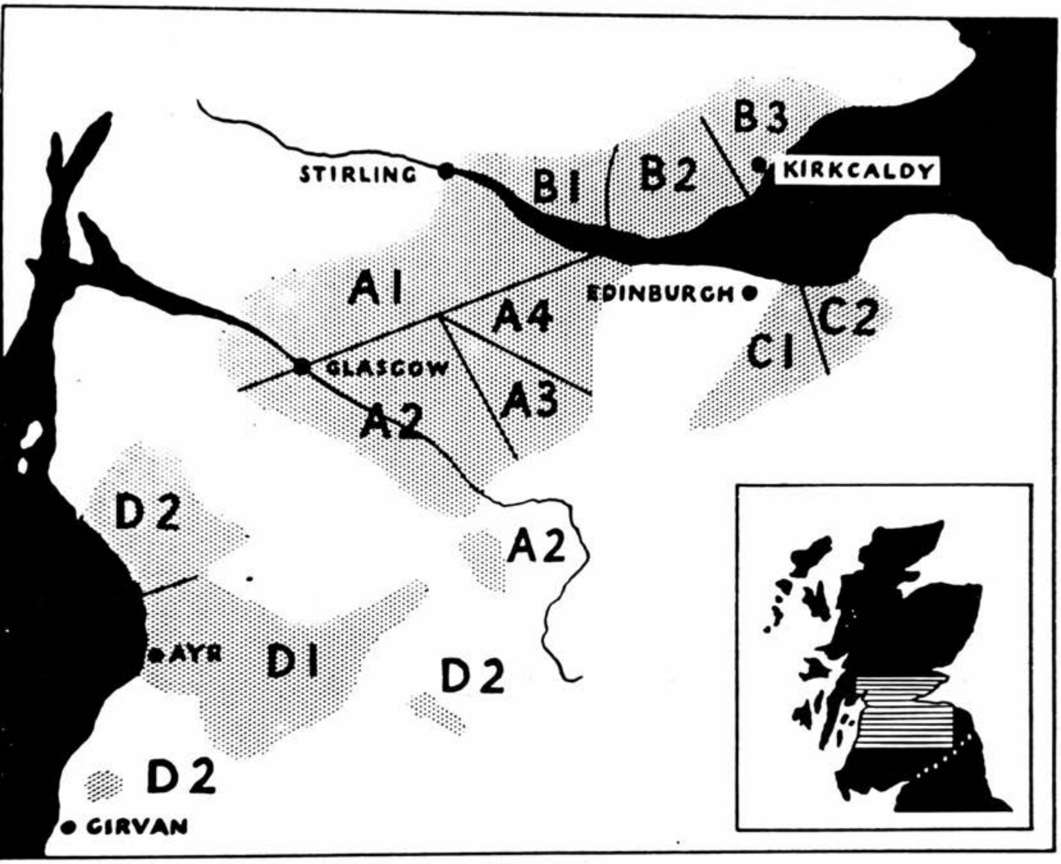
For information about the conditions within the mines and the incidence of pneumoconiosis, I am much indebted to Dr. C. G. Gooding, Senior Medical Officer of the Scottish Division.

The coal is mainly bituminous and the mines are neither excessively wet nor dusty. Although the airborne dust concentrations are now within the approved limits, there is little information about the dust concentrations before 1950 which would be the more important period in relation to the development of pneumoconiosis in the miners of this study. There is no history, however, of notoriously dusty pits in this area.

Since the seams of coal tend to be thin, "faulting" is frequent. This results in more rock work and an increase in the amount of airborne dust of higher silica content. In East Fife (B3) the coal seams are thicker and a coal roof may be left after extraction of coal, thus resulting in less rock work. In this connection, it is of interest that there is a relatively low incidence of pneumoconiosis in this area.

In Central Fife (B2), the National Coal Board have carried out radiological surveys in four small pits around Lochgelly and Cowdenbeath, X-raying over 1700 men. They found an incidence of 2.7% for pneumoconiosis of category 2 or more which included 0.34% with P.M.F. There was a further incidence of 5.3% for category 1. The numbers of those with P.M.F. is an underestimate of the true prevalence, since some are sure to have left the mines earlier for this reason. The incidence in East Fife was found to be about half that of Central Fife.

Figure 33



Scottish coalfields and subdivisions (reproduced from Black, J., 1953, Brit. J. industr. Med., 10, 101).

TABLE I

Name	Age	Source	X-ray category	Associated disease (including E.C.G. abnormalities)	Dyspnoea grade	Smoking habit
R.S.	46	Fitness Centre	1--/-	Cartilage injury: old myocardial infarct	1	S2
J.A.	47	" "	1--/-	Cartilage injury: chronic bronchitis	2	S2
J.H.	50	" "	1--/-	Arm injury: old myocardial infarct	2	(ES)
J.H.	52	" "	1--/-	Fractured ankle: chronic bronchitis	2	S2
R.W.	52	" "	1--/-	Backache	2	(ES)
R.P.	53	" "	2A-/2	Backache: chronic bronchitis	3	S1
J.P.	53	" "	1--/-	Fractured wrist: chronic bronchitis	3	S2
T.S.	54	" "	2--/-	Prolapsed lumbar disc	1	OS
W.A.	54	" "	2--/-	Angina: old myocardial infarct	(1)	S2
H.B.	57	" "	1--/-	Prolapsed lumbar disc	2	S2
W.M.	58	" "	3A1/-	Dupuytren's contracture: peptic ulcer: chronic bronchitis	3	S1
J.J.	59	" "	3C4/4	Peptic ulcer: rheumatoid arthritis: chronic bronchitis	(3)	S1
R.K.	60	" "	3A1/-	Fractured pelvis: chronic bronchitis	(2)	S2
W.L.	61	" "	1--/-	Cervical disc injury: lower limb spasticity	(2)	S2
J.R.	61	" "	1--/-	Back injury: chronic bronchitis	3	ES
D.M.	67	" "	2--/-	Cartilage injury: arthritis of hip: chronic bronchitis	(1)	S2
D.K.	39	Home	2--/-	None	1	S2
H.M.	49	"	2A-/1	"	3	S2
P.M.	58	"	3--/-	"	3	S2
R.W.	60	"	3--/-	"	2	OS
A.F.	60	"	2C3/1	Chronic bronchitis	3	S3
E.L.	60	"	2A1/-	None	2	S2
P.J.	61	"	3--/-	Chronic bronchitis	2	S1
T.W.	64	"	2--/-	None	2	S1
G.T.	66	"	2--/-	"	3	S1
T.C.	67	"	2--/-	"	3	S2

TABLE I (Contd.)

Name	Age	Source	X-ray category	Associated disease (including E.C.G. abnormalities)	Dyspnoea grade	Smoking habit
A.A.	47	I.C.D.U.	1--/-	None	2	S3
W.F.	48	"	1--/-	"	2	S2
J.H.	49	"	1--/-	"	2	S2
L.W.	49	"	2A2/1	"	2	S2
A.J.	52	"	1--/-	"	1	S2
A.N.	52	"	1--/-	"	3	ES
W.M.	52	"	1--/-	Chronic bronchitis	4	S1
W.Y.	53	"	2--/-	None	3	OS
W.S.	54	"	2A2/-	Chronic bronchitis	2	S2
R.B.	54	"	1--/-	Chronic bronchitis: myocardial ischaemia	5	S1
W.W.	55	"	3A1/2	Sinusitis: chronic bronchitis	2	S2
J.S.	55	"	3--/-	Sinusitis: chronic bronchitis	3	S2
W.M.	56	"	2--/-	Myxoedema with E.C.G. changes	3	OS
H.M.	56	"	2--/-	Sinusitis: chronic bronchitis	2	S2
J.S.	57	"	2--/-	Chronic bronchitis	2	OS
P.A.	59	"	2A1/-	None	2	S2
T.M.	62	"	2--/-	"	2	OS
C.P.	63	"	2C2/2	Chronic bronchitis	3	ES
D.M.	63	"	3D4/3	None	5	S2
T.W.	64	"	2--/-	Chronic bronchitis: right bundle branch block	2	S2
J.C.	64	"	1--/-	None	1	OS
P.S.	69	"	3A2/1	Chronic bronchitis	3	S1
R.G.	58	Glenlomond Hospital	3B1/1	Chronic bronchitis	2	S1
J.S.	59	"	3A1/-	Chronic bronchitis	3	S2
D.G.	60	"	3B2/1	None	3	S1
J.C.	64	"	2B2/1	Chronic bronchitis: myocardial ischaemia	3	S1

I.C.D.U. = Industrial Chest Diseases Unit, Bridge of Earn Hospital.

Grades in parenthesis are provisional.

X-ray category, dyspnoea and smoking grades explained in text.

TABLE II

Industrial History

Name	Age	X-ray category	Yrs. in mines	Yrs. on stone-work
R.S.	46	1--/-	17	-
A.A.	47	"	32	-
J.A.	47	"	32	6
W.F.	48	"	29	5
J.H.	49	"	34	-
J.H.	50	"	35	6
J.H.	52	"	28	10
R.W.	52	"	38	-
A.J.	52	"	37	8
W.M.	52	"	36	-
A.N.	52	"	37	-
J.P.	53	"	35	-
R.B.	54	"	39	-
H.B.	57	"	42	-
J.R.	61	"	46	-
W.L.	61	"	38	-
J.C.	64	"	48	-
D.K.	39	2--/-	24	-
W.Y.	53	"	38	-
T.S.	54	"	37	-
W.A.	54	"	36	-
H.M.	56	"	40	-
W.M.	56	"	39	7
J.S.	57	"	42	-
T.M.	62	"	37	-
T.W.	64	"	45	-
T.W.	64	"	50	-
G.T.	66	"	50	-
T.C.	67	"	46	12
D.M.	67	"	49	-

TABLE II (Contd.)

Name	Age	X-ray category	Yrs. in mines	Yrs. on stone-work
J.S.	55	3--/-	39	24
P.M.	58	"	39	-
R.W.	60	"	44	4
P.J.	61	"	45	2
H.M.	49	2A-/1	35	5
L.W.	49	2A2/1	32	4
R.P.	53	2A-/2	39	-
W.S.	54	2A2/-	40	-
W.W.	55	3A1/2	40	-
W.M.	58	3A1/-	44	18
P.A.	59	2A1/-	40	-
J.S.	59	3A1/-	45	3
E.L.	60	2A1/-	45	17
R.K.	60	3A1/-	45	-
P.S.	69	3A2/1	35	-
R.G.	58	3B1/1	42	5
J.J.	59	3C4/4	31	15
A.F.	60	2C3/1	45	-
D.G.	60	3B2/1	46	-
D.M.	63	3D4/3	44	16
C.P.	63	2C2/2	43	16
J.C.	64	2B2/1	35	-

TABLE III

Diffusing capacity, haemoglobin and venous CO_2

Name	Age	X-ray category	DL_{CO} ml/min/mmHg	Hb G%	Venous CO_2 mM/litre
R.S.	46	1--/-	30.0	16.0	31.4
A.A.	47	"	30.1	15.9	34.4
J.A.	47	"	32.9	17.3	28.2
W.F.	48	"	19.7	17.0	30.8
J.H.	49	"	20.3	16.4	29.1
J.H.	50	"	28.3	16.6	32.2
J.H.	52	"	25.4	13.0	31.0
R.W.	52	"	23.9	16.6	(32.7)
A.J.	52	"	31.2	17.2	35.0
W.M.	52	"	28.6	15.0	(33.4)
A.N.	52	"	-	15.0	28.9
J.P.	53	"	20.6	17.4	32.0
R.B.	54	"	20.8	16.7	41.5
H.B.	57	"	23.2	15.8	32.2
J.R.	61	"	26.7	14.2	30.3
W.L.	61	"	23.2	15.0	27.8
J.C.	64	"	29.4	17.0	33.7
D.K.	39	2--/-	21.8	14.8	32.0
W.Y.	53	"	49.1	16.0	37.3
T.S.	54	"	27.9	15.8	30.6
W.A.	54	"	22.2	15.5	34.9
H.M.	56	"	26.0	15.0	30.1
W.M.	56	"	25.9	12.6	31.4
J.S.	57	"	15.8	15.8	(32.2)
T.M.	62	"	25.1	15.0	31.5
T.W.	64	"	21.3	16.1	31.7
T.W.	64	"	21.7	15.5	32.2
G.T.	66	"	17.3	15.4	31.5
T.C.	67	"	16.1	14.5	28.7
D.M.	67	"	22.5	15.8	30.2

TABLE III (Contd.)

Name	Age	X-ray category	DL_{CO} ml/min/mmHg	Hb G%	Venous CO_2 mM/litre
J.S.	55	3--/-	11.0	13.0	29.7
P.M.	58	"	9.4	13.0	31.3
R.W.	60	"	21.6	14.8	31.6
P.J.	61	"	19.8	14.8	33.8
H.M.	49	2A-/1	26.8	15.8	31.0
L.W.	49	2A2/1	33.0	16.4	30.1
R.P.	53	2A-/2	14.7	14.4	31.0
W.S.	54	2A2/-	33.6	14.6	31.2
W.W.	55	3A1/2	19.1	14.4	31.3
W.M.	58	3A1/-	21.5	14.0	29.9
P.A.	59	2A1/-	27.4	14.7	30.7
J.S.	59	3A1/-	24.3	14.6	29.9
E.L.	60	2A1/-	22.1	15.3	31.3
R.K.	60	3A1/-	17.2	14.5	32.5
P.S.	69	3A2/1	14.3	14.1	32.5
R.G.	58	3B1/1	21.5	16.1	41.2
J.J.	59	3C4/4	16.1	12.6	(32.8)
A.F.	60	2C3/1	9.4	14.1	30.0
D.G.	60	3B2/1	22.7	14.6	32.5
D.M.	63	3D4/3	7.3	16.4	34.0
C.P.	63	2C2/2	15.3	16.4	27.7
J.C.	64	2B2/1	18.9	15.0	33.0

Values in parenthesus were not obtained experimentally, but are statistical estimates for purpose of analysis.

DL_{CO} = diffusing capacity of the lungs for carbon monoxide.

TABLE IV

Ventilatory function and lung compliance

Name	Age	X-ray category	Ind. M.B.C. L/min.	M.E.F.R. L/min.	M.I.F.R. L/min.	M.E.F.R. / M.I.F.R.	Compliance ml/cm H_2O
R.S.	46	1--/-	161	534	508	1.05	317
A.A.	47	"	127	483	377	1.28	209
J.A.	47	"	116	565	405	1.40	237
W.F.	48	"	130	395	214	1.85	263
J.H.	49	"	128	457	285	1.60	-
J.H.	50	"	148	456	408	1.12	431
J.H.	52	"	105	374	363	1.03	306
R.W.	52	"	75	190	137	1.39	220
A.J.	52	"	119	562	253	2.22	-
W.M.	52	"	63	136	104	1.31	371
A.N.	52	"	52	93	149	0.63	237
J.P.	53	"	109	409	157	2.60	325
R.B.	54	"	26	29	147	0.20	187
H.B.	57	"	55	100	384	0.26	215
J.R.	61	"	62	286	356	0.80	181
W.L.	61	"	71	191	164	1.16	-
J.C.	64	"	108	471	402	1.17	169
D.K.	39	2--/-	161	707	276	2.56	-
W.Y.	53	"	27	26	261	0.10	151
T.S.	54	"	93	348	186	1.87	216
W.A.	54	"	100	492	412	1.19	-
H.M.	56	"	112	391	234	1.67	-
W.M.	56	"	148	269	317	0.85	-
J.S.	57	"	88	333	260	1.27	97
T.M.	62	"	106	328	163	2.01	208
T.W.	64	"	79	290	184	1.58	-
T.W.	64	"	80	209	144	1.45	446
G.T.	66	"	68	182	122	1.49	-
T.C.	67	"	87	236	199	1.19	-
D.M.	67	"	98	419	295	1.42	180

TABLE IV (Contd.)

Name	Age	X-ray category	Ind. M.B.C. L/min.	M.E.F.R. L/min.	M.I.F.R. L/min.	M.E.F.R. / M.I.F.R.	Compliance ml/cm H_2O
J.S.	55	3--/-	105	512	250	2.04	135
P.M.	58	"	78	306	213	1.43	-
R.W.	60	"	86	277	241	1.15	-
P.J.	61	"	94	408	360	1.13	-
H.M.	49	2A-/1	107	328	228	1.44	-
L.W.	49	2A2/1	81	225	242	0.93	375
R.P.	53	2A-/2	57	116	191	0.84	278
W.S.	54	2A2/-	119	586	277	2.11	385
W.W.	55	3A1/2	95	313	206	1.52	166
W.M.	58	3A1/-	85	175	203	0.86	-
P.A.	59	2A1/-	106	170	308	0.55	307
J.S.	59	3A1/-	102	328	195	1.68	147
E.L.	60	2A1/-	59	86	168	0.51	-
R.K.	60	3A1/-	77	262	249	1.05	331
P.S.	69	3A2/1	86	266	310	0.86	355
R.G.	58	3B1/1	55	108	114	0.95	133
J.J.	59	3C4/4	63	163	175	0.94	291
A.F.	60	2C3/1	56	98	181	0.54	-
D.G.	60	3B2/1	113	414	150	2.76	179
D.M.	63	3D4/3	50	83	273	0.30	207
C.P.	63	2C2/2	90	211	241	0.88	-
J.C.	64	2B2/1	69	165	180	0.92	336

M.E.F.R. = maximum expiratory flow rate.
M.I.F.R. = maximum inspiratory flow rate.

TABLE V

Lung volumes

Name	Age	Surface area M^2	X-ray category	V.C. ml	R.V. ml	T.L.C. ml	$\frac{R.V.}{T.L.C.}$ %
R.S.	46	1.67	1--/-	5710	2070	7780	27
A.A.	47	1.84	"	5428	3434	8862	39
J.A.	47	1.79	"	4750	2950	7700	38
W.F.	48	1.78	"	5434	4132	9566	43
J.H.	49	1.75	"	4167	2462	6629	37
J.H.	50	1.98	"	5900	3095	8995	34
J.H.	52	1.83	"	3560	3580	7140	50
R.W.	52	1.70	"	3590	2950	6540	45
A.J.	52	1.80	"	4949	3631	8580	42
W.M.	52	1.88	"	3000	4118 (1)	7118	58
A.N.	52	1.80	"	3370	4676	8046	38
J.P.	53	1.78	"	3783	3980	7763	51
R.B.	54	1.84	"	2774	4634	7408	63
H.B.	57	1.58	"	4234	3710	7944	47
J.R.	61	1.87	"	3480	3410 (1)	6890	50
W.L.	61	1.72	"	3760	3820	7580	50
J.C.	64	1.87	"	4776	2651 (1)	7427	36
D.K.	39	1.77	2--/-	5129	2277	7406	31
W.Y.	53	1.94	"	2988	5254	8242	64
T.S.	54	1.6	"	3210	1840 (1)	5050	36
W.A.	54	2.10	"	4279	2316	6595	35
H.M.	56	1.75	"	3629	2436	6065	40
W.M.	56	1.72	"	5130	1530	6660	23
J.S.	57	1.62	"	2485	1944	4429	44
T.M.	62	1.60	"	3537	2038	5575	37
T.W.	64	1.78	"	3412	2150	5562	39
T.W.	64	1.55	"	4071	4056	8127	51
G.T.	66	1.73	"	2295	2913	5208	56
T.C.	67	1.64	"	3925	3637	7562	48
D.M.	67	1.81	"	3977	3667	7644	48

TABLE V (Contd.)

Name	Age	Surface area M^2	X-ray category	V.C. ml	R.V. ml	T.L.C. ml	$\frac{R.V.}{T.L.C.}$ %
J.S.	55	1.61	3--/-	3781	2111 (1)	5892	36
P.M.	58	1.54	"	2550	2099	4649	45
R.W.	60	1.63	"	4205	2335	6540	36
P.J.	61	1.75	"	3961	3344	7305	46
H.M.	49	1.80	2A-/1	4498	2759	7257	38
L.W.	49	1.86	2A2/1	5175	3598	8773	41
R.P.	53	1.83	2A-/2	3799	4766	8565	56
W.S.	54	1.79	2A2/-	5459	4178	9637	43
W.W.	55	1.54	3A1/2	3778	2199	5977	37
W.M.	58	1.87	3A1/-	4100	2150	6250	34
P.A.	59	1.74	2A1/-	4613	2984 (1)	7597	38
J.S.	59	1.85	3A1/-	3698	2836	6534	43
E.L.	60	1.91	2A1/-	2973	2392	5365	45
R.K.	60	1.61	3A1/-	3064	3021	6085	50
P.S.	69	1.61	3A2/1	4678	2842 (1)	7520	38
R.G.	58	1.55	3B1/1	2802	2796	5598	50
J.J.	59	1.75	3C4/4	3530	2600	6130	42
A.F.	60	1.63	2C3/1	4181	3935	8116	49
D.G.	60	1.94	3B2/1	3464	2142	5606	38
D.M.	63	1.49	3D4/3	4469	2153	6622	33
C.P.	63	1.90	2C2/2	4976	1807	6783	27
J.C.	64	1.78	2B2/1	3733	2350	6083	39

Residual volume (R.V.) is the average of duplicate measurements except those marked (1).